



Saudi Arabia: Promoting Self-Directed Learning in Family Medicine Residency Program in Saudi Arabia page 34

From the Editor

Chief Editor:

A. Abyad
MD, MPH, AGSF, AFCHSE
Email: aabyad@cyberia.net.lb

Ethics Editor and Publisher

Lesley Pocock
medi+WORLD International
AUSTRALIA

Email:

lesleypocock@mediworld.com.au

In this issue there are a variety of papers from the region discussing wide topics of interest to medical specialty and primary health care.

A paper from Saudi Arabia examined fostering self-directed learning (SDL) in residency program in family medicine in Saudi Arabia. It investigated the most effective ways to help in appropriate application of Self-directed learning in residency program. Learning is maximized when it is self-directed so that residents study material that is most relevant to them. Medical residents learn best when they learn according to their perceived needs and competency gaps which (learner-centered needs and gaps) more than teacher-centered ones. Residents engage in self-directed learning by first identifying a clinical problem, then pursuing the learning task, next acquiring the new knowledge or skill, and finally practicing the new knowledge or skill. In this paper, I have described a curricular intervention that employs several educational and administrative modalities to foster the self-direction in learning in family medicine training program in Saudi Arabia.

A paper from Turkey looked at Cholelithiasis may also be a consequence of metabolic syndrome. The study was performed in Internal Medicine Polyclinics on routine check up patients. All cases with cholelithiasis or already performed cholecystectomy for cholelithiasis were put into the first and age and sex-matched control cases were put into the second groups. One hundred and forty-four cases either with cholelithiasis or already performed cholecystectomy for cholelithiasis were detected among 3,437 cases, totally (4.1%). One hundred and sixteen (80.1%) of them were female with a mean age of 53.6 years. Obesity was significantly higher (54.8% versus 43.7%, $p < 0.01$). There are significant relationships between cholelithiasis and parameters of the metabolic syndrome including female predominance, elder age, BMI, obesity, hypertension, and hypertriglyceridemia. On the other hand, the significantly lower

prevalence of hyperbetalipoproteinemia in the cholelithiasis patients should be researched with further studies.

Baradaran et al looked at SUMO1 pseudogene 3 (SUMO1P3) expression in human gastric cancer and its clinical significances. Fresh gastric cancer and adjacent non-tumor tissues were collected from 182 GC patients, who admitted to the Alzahra Hospital, Isfahan, Iran. Quantitative reverse transcription-polymerase chain reaction was used to investigate the SUMO1P3 levels. Then, the association between the level of SUMO1P3 in gastric cancer tissues and the clinicopathological features of patients with gastric cancer was analyzed. The results showed that SUMO1P3 levels in male were not significantly higher than those in female ($p = 0.485$). No significant deference of SUMO1P3 expression was observed between patients under 64 years old and above ($p = 0.155$). The SUMO1P3 levels were not associated with perineural invasion ($p = 0.319$), lymphatic invasion ($p = 0.797$), invasion depth ($p = 0.790$), location of the tumor ($p = 0.811$), tumor size ($p = 0.635$), and grading ($p = 0.289$). The authors concluded that these results indicated that in our patient population and according to the used method in this study, pseudogene-expressed lncRNA SUMO1P3 may not be a potential biomarker in the diagnosis of gastric cancer.

A medical record review that was performed at Lahey Hospital Medical Center (Jordan), medical records in the period between 12/2003 and 12/2013 were reviewed, 1098 medical records were reviewed, those were carrying diagnosis OF Herpetic Eye Disease (HED) and were divided into 2 groups according to the etiological agent: Herpes Simplex virus (HSV) ($n=473$), Varicella Zoster Virus (VZV) ($n=625$). The groups were evaluated for the age at diagnosis and the etiologies of elevated Intra ocular Pressure (IOP), whether its HED related (trabeculitis, steroid response), or non HED Glaucoma Related Diagnosis. Although many of the features between HSV and VZV subgroups are similar, the VZV group was older and appeared to have more prolonged hypertensive course than the HSV group. 4.3% of patients with HED have significant elevated IOP directly related to disease or treatment. Secondary glaucoma is a consequence of Herpetic Eye disease, but fortunately surgical intervention is rarely required to control IOP.

A paper from Iran looked whether Decoy Cell Viruria in Kidney Transplant Patients. correlate with Renal Function? This analytic cross-sectional study conducted in Transplant Center of Alzahra Hospital, Isfahan, Iran between Jun 2014 and June 2015. Clinical screening for polyomavirus infection done by means of urine cytological evaluation for decoy cells. Urine samples were analyzed in three steps including 2-4 months after transplantation, three and six months later. Thirty-three patients (22 male and 11 female) received kid-

ney transplant from living donors. The average of patients' age was 41.9 ± 12.83 (range: 20-63 years). Peritoneal and hemodialysis were used for 15.6% and 84.4% of recipients. The occurrence of decoy cell viruria at the time of enrollment, 3 and 6 months later found in 18.2%, 10.7% and zero, respectively. The authors concluded that urine cytology is easy to perform and of low cost, it is a useful tool for the investigation of active polyoma virus infection. Moreover, the findings advocate that the presence of decoy cells along with high creatinine is a better indicator of the virus presence.

Azadi et al looked at Gum Sisymbrium irio effect on the quality attributes of baguettes. In this study, gum Sisymbrium irio at different levels of Control, 1/0, 1/5 and 2/0 percent and wheat flour, in loaf bread and its impact on the quality attributes including technological features, colours and staling throughout the day, various storage mechanisms were evaluated. The results of the evaluation of technical features, showed that gum Sisymbrium irio increased humidity, reduced stiffness and reduced bran volume compared with the control bread. By increasing the hold time, stale bread and buns control treated with different levels of gum Sisymbrium irio significantly increased.

Fazel et al attempted to determine how frequently pregnant asthmatics are sensitive to food and inhalation allergen. Euroimmun tests were performed to identify the prevalence of sensitivity towards allergens among pregnant asthmatics. A total of 1,603 women were selected from those who had visited Mobini Hospital in Iran August 2014-April 2015. The authors drew blood samples from these women and, postpartum, from their infants. These were used to measure IgE and RAST to inhalation and food allergens. Descriptive and comparative statistical analyses were performed. The results were analyzed using SPSS version 20. A total of 1,603 pregnant women referred to Mobini Hospital - Iran were included in the analysis. Thirty-four pregnant asthmatics were confirmed as having asthma. The authors concluded that their results suggest that there is no association of some inhalation and food allergens with maternal and fetal IgE. Forthcoming studies should take this into account, i.e. trying to detect different local allergens that perhaps have potential maternofetal transfer.

Copyright

While all efforts have been made to ensure the accuracy of the information in this journal, opinions expressed are those of the authors and do not necessarily reflect the views of The Publishers, Editor or the Editorial Board. The publishers, Editor and Editorial Board cannot be held responsible for errors or any consequences arising from the use of information contained in this journal; or the views and opinions expressed.

2 Editorial

DOI: 10.5742/ MEWFM.2017.92959

Original Contribution/Clinical Investigation**4 <-- Jordan, USA -->****Herpetic Eye Disease and Glaucoma Related Diagnosis****C. Dan Earley, Amal M Althawabi, Paul R Cotran, Sarkis H Soukiasian**

DOI: 10.5742/ MEWFM.2017.92960

9 <-- Turkey, Lebanon, Australia -->**Cholelithiasis may also be a consequence of metabolic syndrome****Mehmet Rami Helvaci, Mursel Davarci, Orhan Veli Ozkan, Ersan Semerci, Abdulrazak Abyad, Lesley Pocock**

DOI: 10.5742/ MEWFM.2017.92961

14 <-- Iran -->**SUMO1 pseudogene 3 (SUMO1P3) expression in human gastric cancer and its clinical significance****Hamid Reza Baradaran-Ghahfarokhi, Habib Malekpour,****Ehsan Nazemalhosseini Mojarad, Hamid Asadzadeh Aghdaei, Majid Asadi-Samani**

DOI: 10.5742/ MEWFM.2017.92962

20 <-- Iran -->**Decoy Cell Viruria in Kidney Transplant Patients. Does it correlate with Renal Function?****Akram Abedi, Mojgan Mortazavi, Omid Mirmosayyeb, Shahram Taheri,****Nooshin Afsharmoghadam, Majid Asadi-Samani, Shahram Sajadie, Azar Baradaran**

DOI: 10.5742/ MEWFM.2017.92963

26 <-- Iran, Austria -->**To determine how frequently pregnant asthmatics are sensitive to food and inhalation allergens****Nasrin Fazel, Michael Kundi, Erika Jensen-Jarolim, Isabella Maria Pali-Schöll,****Asghar Kazemzadeh, Mojtaba Fattahi Abdizadeh, Habibollah Esmaily,****Roya Akbarzadeh, Raheleh Ahmadi**

DOI: 10.5742/ MEWFM.2017.92964

Special Education Feature**34 <-- Saudi Arabia -->****Promoting Self-Directed Learning in Family Medicine Residency Program in Saudi Arabia****Mohammed H Doghether**

DOI: 10.5742/ MEWFM.2017.92965

International Health Affairs**44 <-- Iran -->****Gum Sisymbrium irio effect on the quality attributes of baguettes****Leila Azadi, Mohammad Hojjatoleslami, Hooman Molavi**

DOI: 10.5742/ MEWFM.2017.92966

Herpetic Eye Disease and Glaucoma Related Diagnosis

C. Dan Earley (1)

Amal M Althawabi (1,3)

Paul R Cotran (1,2)

Sarkis H Soukiasian (1,2)

(1) Dept. of Ophthalmology, Lahey Clinic, Burlington, MA

(2) Dept. of Ophthalmology, Tufts Medical Center, Boston, MA

(3) Royal Medical Services, King Hussein Medical Center, Amman, Jordan.

Correspondence:

Dr. Amal Al-Thawabi

Cornea and refractive surgery specialist in King Hussein Medical Center

Amman,

Jordan

Email: aalthawabi@hotmail.com

Abstract

This is a medical record review that was performed at Lahey Hospital Medical Center. Medical records in the period between 12/2003 and 12/2013 were reviewed; 1098 medical records were reviewed, those who were carrying diagnosis of Herpetic Eye Disease (HED) were divided into 2 groups according to the etiological agent: Herpes Simplex virus (HSV) (n=473) , Varicella Zoster Virus (VZV) (n=625).

The groups were evaluated for the age at diagnosis and the etiologies of elevated Intra ocular Pressure (IOP), whether it was HED related (trabeculitis, steroid response), or non HED Glaucoma Related Diagnosis.

Although many of the features between HSV and VZV subgroups are similar, the VZV group was older and appeared to have more prolonged hypertensive course than the HSV group.

4.3% of patients with HED have significant elevated IOP directly related to disease or treatment.

Secondary glaucoma is a consequence of Herpetic Eye disease, but fortunately surgical intervention is rarely required to control IOP.

Key words: Herpetic Eye Disease, Glaucoma related diagnosis, Ocular Hypertension, steroid responder.

Objectives

Present the overall incidence of glaucoma related diagnosis (GRD) in a population of patients with herpetic eye disease.

Describe the incidence of glaucoma (GI) or ocular hypertension (OHT) directly attributed to HED or treatment [e.g. steroid response (SR)].

Identify differentiating characteristics of GL, OHT or SR within the HED population (VZV vs HSV).

Introduction

Herpetic eye disease is the most common cause of infectious anterior uveitis seen at tertiary referral centers.(1)

Elevated intraocular pressure may be seen as a presenting or complicating feature of herpetic eye diseases (HED) due to both Varicella Zoster Virus (VZV) and Herpes Simplex Virus (HSV).

Potential mechanisms include decreased outflow due to inflammation of the trabecular meshwork (trabeculitis), outflow blockage due to inflammatory and pigmented debris, as well as a hypertensive response to topical corticosteroids.

Most patients with acute iritis have low IOP. High IOP in a patient with uveitis should raise a high index of suspicion of a herpetic etiology, especially with the presence of other signs such as large greasy KP's, iris transillumination defects and segmental iris atrophy(1).

There are other possible causes for elevated IOP associated with HSV and VZV keratouveitis, Although secondary angle closure may occur due to pupillary block by posterior synechiae, most patients who developed glaucoma had open angles.(2) This is likely attributed to increase in aqueous debris from elevated aqueous proteins, fibrin, and inflammatory cells.(3,4) Consecutive damage to the trabecular meshwork by HSV and VZV infection has also been noticed (12).

Steroid response glaucoma could be another mechanism of IOP elevation associated with herpetic keratouveitis, Treatment with topical steroids will reduce the risk of persistent or progressive stromal keratouveitis, but should be adjusted according to the IOP values after starting steroid treatment.(6,7,8)

The purpose of our study is to present the overall incidence of glaucoma related diagnosis (GRD) in a population of patients with herpetic eye disease; describe the incidence of glaucoma (GI) or ocular hypertension (OHT) directly attributed to HED or treatment [e.g. steroid response (SR)] and to identify differentiating characteristics of GL, OHT or SR within the HED population (VZV vs HSV).

Materials and Methods

This is a retrospective medical records review that was conducted in patients evaluated at the Lahey Hospital and Medical Center Department of Ophthalmology between 12/2003 and 12/2013.

All the records were screened for ICD-9 codes of Herpetic Eye Disease (053.2... and 054.4...).

All medical records of patients with both HED and concurrent GRD codes were reviewed to identify GRD directly attributable to HED or treatment.

Elevated IOP was considered significant if ≥ 25 on two consecutive measurements.

Conclusion

This study specifically separated causes of IOP in Herpetic Eye Disease.

Although many of the features between HSV and VZV subgroups are similar, the VZV group was older and appeared to have a more prolonged hypertensive course than the HSV group.

Surgical intervention was rare, consistent with literature.

Results

1,098 patients were included in our medical review; 57% carried the diagnosis of VZV and 43% had HSV. 32% had Glaucoma related diagnosis (GRD) and Herpetic Eye Disease (HED).

The average age of presentation was 67 years for VZV diagnosis and 58 years for HSV diagnosis.

In the majority of patients, the GRD was not directly related to HED (87% had unrelated glaucoma related diagnosis).

Approximately 4% of all patients with HED had elevated IOP directly related to HED or treatment. (Table 1 - next page).

In only 13% of patients identified with both HED and GRD was the elevated IOP directly related to HED or treatment.

HZV patients appeared older than HSV patients and approached statistical significance.

Chronic elevated IOP (requiring treatment ≥ 3 months) due to inflammation was more often noted with VZV (Figure 1 - next page).

Table 1: shows patient distribution of the total number of medical records reviewed, the number of cases with glaucoma related and unrelated to HED diagnosis, average age of presentation and average age to IOP elevation

	TOTAL (%)	VZV (%)	HSV (%)
Total HED	1098	625 (57%)	473 (43%)
GRD+HED	349 (32%†)	218 (35%†)	131 (28%†)
GRD unrelated to HED (preexisting or post-herpes)	302 (27%)	189 (30%)	113 (24%)
OHT/GL/SR directly related to HED	47 (4.3%*) (13%**)	29 (4.6%*) (13%**)	18 (3.8%*) (14%**)
Ave age (years)	63	67	58
Ave days to inc IOP	143	118	181

HED=Herpetic Eye Disease

GRD-Glaucoma Related Diagnosis

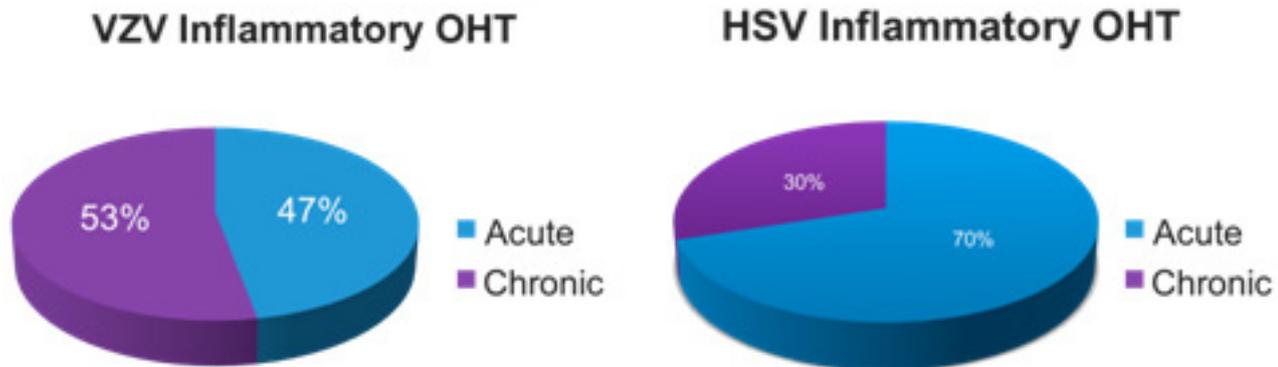
OHT/GL/SR- Ocular Hypertension/ Glaucoma/ Steroid Responder

† % out of Total HED (HSV +VZV)

* % out of Total HED population

** % out of GRD + HED

Figure 1: Rates of Inflammatory OHT (Ocular Hypertension)



Peak IOPs and number of glaucoma medications used were similar between HSV and VZV groups (Data not presented).

We were able to classify the etiologies of increased IOP among this group (Table 2). We found that 2.5% had an inflammatory etiology, 1.4% was due to steroid response and 0.5% was combined effect of inflammatory and steroid response.

Table 2: Etiology of Increased IOP

	TOTAL	VZV	HSV	P value
INFLAMMATORY	27 (2.5%) 14M/13F	17 (2.7%) 10M/7F	10 (2.1%) 4M/6F	NS
Age at HED	64	71	56	p=.07
Days Until OHT	120	67	210	NS
SR	15 (1.4%) 9M/6 F	7 (1.1%), 5M/2F	8, (1.7%) 4M/4F	NS
Age at HED	61	60	62	NS
Days Until OHT	212	263	168	NS
INFLAMMATORY + SR	5 (0.5%) 3M/2F	4 (0.6%) 2M/2F	1* (0.2%) 1M	NS
Age at HED	67	70	57	NS
Days Until OHT	65	80	5*	NS

* 1 Patient

HED=Herpetic Eye Disease

GRD-Glaucoma Related Diagnosis

OHT/GL/SR- Ocular Hypertension/ Glaucoma/ Steroid Responder

† % out of Total HED (HSV +VZV)

* % out of Total HED population

** % out of GRD + HED

Surgical intervention was rare, consistent with the literature.(8)

Table 3: Patients requiring surgical intervention

	HED	VZV	HSV
Inflammatory	3	2	1
Steroid Responders	2	1	1

Discussion

This study specifically separated causes of IOP in HED (Inflammation vs Steroid Response vs Mixed diagnosis).

4.3% of patients with HED have significant elevated IOP directly related to disease or treatment.

Although many of the features between HSV and VZV subgroups are similar, the VZV group was older and appeared to have more prolonged hypertensive course than the HSV group.

Surgical intervention was rare, consistent with literature.

Study limited by retrospective study design.

Some differences between HSV and VZV sub groups approached statistical significance but small study population limited critical statistical evaluation.

Future study of larger population of patients may help better define potential differences between HSV and VZV.

Although by ICD 9 searching 32% of patients with HED had associated GRD, the vast majority were unrelated to herpes.

References

1. Doran, M. Understanding and Treating Viral Anterior Uveitis. EyeNet magazine. 2009 (1); 33-37.
2. Falcon MG, Williams HP. Herpes simplex keratouveitis and glaucoma. Trans Ophthal Soc UK. 1978;98:101-104.
3. Peretz WL, Tomasi TB. Aqueous humor proteins in uveitis. Immuno-electrophoretic and gel diffusion studies on normal and pathological human aqueous humor. Arch Ophthalmol. 1961;65:20-23.
4. Hogan MJ, Kimura SJ, Thygeson P. Pathology of herpes simplex keratouveitis. Trans Am Ophthalmol Soc. 1963;61:75-99.

5. Tiwari V, Clement C, Scanlan P, et al. A role for herpes virus entry mediator as the receptor for herpes simplex virus 1 entry into primary human trabecular meshwork cells. *J Virol.* 2005;79(20):13173-13179.
6. Gorla, M., & Brown, S. (2013). Glaucoma Associated With Herpes Simplex Virus. *Glaucoma Today*, 46-48.
7. Wilhelmus KR, Gee L, Hauck WW, et al. Herpetic Eye Disease Study. A controlled trial of topical corticosteroids for herpes simplex stromal keratitis. *Ophthalmology.* 1994;101:1883-1896.
8. Sungur, G., Hazirolan, D., Yalvac, I., Ozer, P., Aslan, B., & Duman, S. (n.d.). Incidence and prognosis of ocular hypertension secondary to viral uveitis. *International Ophthalmology*, 191-194
9. Wensing, B., Relvas, L., & Caspers, L. (2011). Comparison of rubella virus- and herpes virus-associated anterior uveitis: Clinical manifestations and visual prognosis. *Ophthalmology*, 118(10), 1905-1910.

Cholelithiasis may also be a consequence of metabolic syndrome

Mehmet Rami Helvaci (1)

Mursel Davarci (2)

Orhan Veli Ozkan (3)

Ersan Semerci (3)

Abdulrazak Abyad (4)

Lesley Pocock (5)

(1) Specialist of Internal Medicine, M.D.

(2) Specialist of Urology, M.D.

(3) Specialist of General Surgery, M.D.

(4) Middle-East Academy for Medicine of Aging, Chairman, M.D., MPH, MBA, AGSF

(5) medi-WORLD International

Correspondence:

Mehmet Rami Helvaci, M.D.

07400, ALANYA,

Antalya,

Turkey

Phone: 00-90-506-4708759

Email: mramihelvaci@hotmail.com

Abstract

Background: We tried to understand whether or not there is a significant relationship between cholelithiasis and parameters of the metabolic syndrome.

Methods: The study was performed in Internal Medicine Polyclinics on routine check up patients. All cases with cholelithiasis or already performed cholecystectomy for cholelithiasis were put into the first group and age and sex-matched control cases were put into the second group.

Results: One hundred and forty-four cases either with cholelithiasis or already performed cholecystectomy for cholelithiasis were detected among 3.437 cases, totally (4.1%). One hundred and sixteen (80.1%) of them were female with a mean age of 53.6 years. Obesity was significantly higher (54.8% versus 43.7%, $p<0.01$) and normal weight was significantly lower (7.6% versus 18.0%, $p<0.01$) in the cholelithiasis group, and the mean body mass indexes (BMI) were 31.0 versus 28.9 kg/m² in them, respectively ($p<0.01$). Probably parallel to the higher mean BMI, prevalences of hypertension (26.3%

versus 13.1%, $p<0.001$) and hypertriglyceridemia (25.0% versus 18.0%, $p<0.05$) were also higher in the cholelithiasis group, significantly. On the other hand, hyperbetalipoproteinemia was significantly lower in the cholelithiasis group with unknown reasons (9.7% versus 18.0%, $p<0.05$).

Conclusions: Cholelithiasis is a common pathology in society and nearly four-fold more frequent in women, particularly in their fifties. There are significant relationships between cholelithiasis and parameters of the metabolic syndrome including female predominance, elder age, BMI, obesity, hypertension, and hypertriglyceridemia. On the other hand, the significantly lower prevalence of hyperbetalipoproteinemia in the cholelithiasis patients should be researched with further studies.

Key words: Cholelithiasis, metabolic syndrome, obesity, hyperbetalipoproteinemia

Introduction

Chronic endothelial damage may be the most common type of vasculitis and the leading cause of aging, morbidity, and mortality in human beings. Much higher blood pressure (BP) of the afferent vasculature may be the major underlying cause by inducing recurrent injuries on endothelium, and probably whole afferent vasculature including capillaries, are involved in the process. Thus the term of venosclerosis is not as famous as atherosclerosis in the literature. Secondary to the chronic endothelial inflammation, edema, and fibrosis, vascular walls become thickened, their lumens are narrowed, and they lose their elastic natures that reduce blood flow and increase systolic BP further. Some of the well-known indicators of the inflammatory process are sedentary life style, animal-rich diet, overweight, smoking, alcohol, hypertriglyceridemia, hyperbetalipoproteinemia, dyslipidemia, impaired fasting glucose, impaired glucose tolerance, white coat hypertension, and other chronic inflammatory processes including rheumatologic disorders, prolonged infections, and cancers for the development of irreversible consequences including obesity, hypertension, diabetes mellitus (DM), cirrhosis, peripheral artery disease (PAD), chronic obstructive pulmonary disease (COPD), chronic renal disease (CRD), coronary artery disease (CAD), mesenteric ischemia, osteoporosis, and stroke, all of which terminate with early aging and death. Although early withdrawal of causative factors may prevent final consequences, after development of cirrhosis, COPD, CRD, CAD, PAD, or stroke, endothelial changes cannot be reversed completely due to their fibrotic natures. They were researched under the title of metabolic syndrome in the literature, extensively (1-4). On the other hand, gallstone is also found among one of the most common health problems in developed countries (5), and it is particularly frequent in women above the age of 40 years (6). Most of the gallstones are found in the gallbladder, which is also called cholelithiasis. Its pathogenesis is uncertain and it appears to be influenced by genetic and environmental factors (7). Excess weight is a known and age-independent risk factor for gallstone (8). Delayed bladder emptying, decreased small intestinal motility, and sensitivity to cholecystokinin were associated with obesity and gallstone disease (9). An increased risk was confirmed in obese diabetics with hypertriglyceridemia (10), and plasma cholesterol levels were found related with gallstone (11). Even more conflicting results were reported about an association between gallstone and smoking (12-14). We tried to understand whether or not there is a significant relationship between cholelithiasis and parameters of the metabolic syndrome.

Materials and Methods

The study was performed in Internal Medicine Polyclinics of the Dumlupinar and Mustafa Kemal Universities on routine check up of patients between August 2005 and November 2007. We took consecutive patients below the age of 70 years to avoid debility induced weight loss in elders. Their medical histories, including smoking habit, hypertension, DM, dyslipidemia, and already used medications and

performed operations were learnt, and a routine check up procedure including fasting plasma glucose (FPG), triglyceride, high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), and an abdominal ultrasonography was performed. Patients with devastating illnesses including type 1 DM, malignancies, acute or chronic renal failure, chronic liver diseases, hyper- or hypothyroidism, and heart failure were excluded to avoid their possible effects on weight. Current daily smokers for the last six months and cases with a history of five pack-years were accepted as smokers. Cigar or pipe smokers were excluded. Body mass index (BMI) of each case was calculated by the measurements of the same physician instead of verbal expressions since there is evidence that heavier individuals systematically underreport their weight (15). Weight in kilograms is divided by height in meters squared, and underweight is defined as a BMI of lower than 18.5, normal weight as 18.5-24.9, overweight as 25.0-29.9, and obesity as a BMI of 30.0 kg/m² or greater (16). Cases with an overnight FPG level of 126 mg/dL or greater on two occasions or already receiving antidiabetic medications were defined as diabetics (16). An oral glucose tolerance test with 75-gram glucose was performed in cases with a FPG level between 110 and 125 mg/dL, and diagnosis of cases with a 2-hour plasma glucose level 200 mg/dL or greater is DM (16). Patients with dyslipidemia were detected, and we used the National Cholesterol Education Program Expert Panel's recommendations for defining dyslipidemic subgroups (16). Dyslipidemia is diagnosed when LDL-C is 160 or higher and/or TG is 200 or higher and/or HDL-C is lower than 40 mg/dL. Office BP was checked after a 5-minute rest in seated position, with a mercury sphygmomanometer on three visits, and no smoking was permitted during the previous 2 hours. A 10-day twice daily measurement of blood pressure at home (HBP) was obtained in all cases, even in normotensives in the office due to the risk of masked hypertension after a 10-minute education session about proper BP measurement techniques (17). The education included recommendation of upper arm while discouraging wrist and finger devices, using a standard adult cuff with bladder sizes of 12 x 26 cm for arm circumferences up to 33 cm in length and a large adult cuff with bladder sizes of 12 x 40 cm for arm circumferences up to 50 cm in length, and taking a rest at least for a period of 5 minutes in the seated position before measurement. An additional 24-hour ambulatory BP monitoring was not required due to the equal efficacy of the method with HBP measurement to diagnose hypertension (18). Eventually, hypertension is defined as a BP of 135/85 mmHg or greater on HBP measurements (17). Cholelithiasis was diagnosed ultrasonographically. Eventually, all cases either with presenting cholelithiasis or already performed cholecystectomy for cholelithiasis were put into the first group and age and sex-matched control cases were put into the second groups. Prevalences of smoking, normal weight, overweight, obesity, hypertension, DM, hypertriglyceridemia, hyperbetalipoproteinemia, and dyslipidemia and mean BMI values were detected in both groups and compared in between. Mann-Whitney U test, Independent-Samples t test, and comparison of proportions were used as the methods of statistical analyses.

Results

Although the exclusion criteria, 119 cases with cholecystectomy for cholelithiasis and 25 with already presenting asymptomatic cholelithiasis were detected among 3,437 cases, total (4.1%). One hundred and sixteen (80.1%) of them were female with a mean age of 53.6 years, so cholelithiasis is mainly a disorder of females in their fifties. Prevalences of smoking were similar in the cholelithiasis and control groups (18.0% versus 19.4%, $p>0.05$, respectively). There was not any patient with underweight. Interestingly, 92.3% (133 cases) of the cholelithiasis group had excess weight and only 7.6% (11 cases) of them had normal weight. Obesity was significantly higher (54.8% versus 43.7%, $p<0.01$) and normal weight was significantly lower (7.6% versus 18.0%, $p<0.01$) in the cholelithiasis group. Mean BMI values were 31.0 and 28.9 kg/m², ($p<0.01$) in them. Probably parallel to the higher mean BMI, prevalences of hypertension (26.3% versus 13.1%, $p<0.001$) and hypertriglyceridemia (25.0% versus 18.0%, $p<0.05$) were also higher in the cholelithiasis group, significantly. Differences were nonsignificant according to the prevalences of DM and dyslipidemia. On the other hand, hyperbetalipoproteinemia was significantly lower in the cholelithiasis group with unknown reasons (9.7% versus 18.0%, $p<0.05$) (Table 1).

Table 1: Comparison of cases with and without cholelithiasis

Variable	Cases with cholelithiasis or cholecystectomy for cholelithiasis	Control cases	p-value
Number	144	144	
Female ratio	80.5% (116)	80.5% (116)	
Mean age (year)	53.6 ± 9.3 (27-70)	53.6 ± 10.2 (28-70)	Ns*
Prevalence of smoking	18.0% (26)	19.4% (28)	Ns
<u>Mean BMI† (kg/m²)</u>	<u>31.0 ± 6.1 (19-51)</u>	<u>28.9 ± 5.7 (19-52)</u>	<u><0.01</u>
<u>Prevalence of normal weight</u>	<u>7.6% (11)</u>	<u>18.0% (26)</u>	<u><0.01</u>
Prevalence of overweight	37.5% (54)	38.1% (55)	Ns
<u>Prevalence of obesity</u>	<u>54.8% (79)</u>	<u>43.7% (63)</u>	<u><0.01</u>
<u>Prevalence of hypertension</u>	<u>26.3% (38)</u>	<u>13.1% (19)</u>	<u><0.001</u>
Prevalence of DM‡	20.8% (30)	19.4% (28)	Ns
<u>Prevalence of hyperbetalipoproteinemia</u>	<u>9.7% (14)</u>	<u>18.0% (26)</u>	<u><0.05</u>
<u>Prevalence of hypertriglyceridemia</u>	<u>25.0% (36)</u>	<u>18.0% (26)</u>	<u><0.05</u>
Prevalence of dyslipidemia	31.9% (46)	29.8% (43)	Ns

*Nonsignificant ($p>0.05$)

†Body mass index

‡Diabetes mellitus

Discussion

Excess weight leads to both structural and functional abnormalities of many organ systems of the body. Recent studies revealed that adipose tissue produces biologically active leptin, tumor necrosis factor- α , plasminogen activator inhibitor-1, and adiponectin which are closely related with the development of complications (19). For instance, the cardiovascular field has recently shown a great interest in the role of inflammation in development of atherosclerosis and numerous studies indicated that inflammation plays a significant role in the pathogenesis of atherosclerosis and thrombosis (20, 21). Adipose tissue is involved in the regulation of cytokines (22). On the other hand, individuals with excess weight will have an increased circulating blood volume as well as an increased cardiac output, thought to be the result of increased oxygen demand of the excessive fat tissue. The prolonged increase in circulating blood volume can lead to myocardial hypertrophy and decreased compliance, in addition to the common comorbidity of hypertension. In addition to the hypertension, the prevalences of high FPG, high serum total cholesterol, and low HDL-C, and their clustering were all raised with the higher BMI (23). Combination of these cardiovascular risk factors will eventually lead to an increase in left ventricular stroke with higher risks of arrhythmias, cardiac failure, and sudden cardiac death. Similarly, the incidences of CHD and stroke have increased with a higher BMI in the other studies (23, 24), and risk of death from all causes including cancers increases throughout the range of moderate and severe excess weight for both genders in all age groups (25). As another consequence of excess weight on health, the cholelithiasis cases had a significantly higher mean BMI in the present study (31.0 versus 28.9 kg/m², $p < 0.01$) similar to the previous reports (8, 9). Probably as a consequence of the significantly higher BMI, the prevalences of hypertension (26.3% versus 13.1%, $p < 0.001$) and hypertriglyceridemia (25.0% versus 18.0%, $p < 0.05$) were also higher in the cholelithiasis patients. The relationship between excess weight and elevated BP and hypertriglyceridemia is already described in the metabolic syndrome (26), and clinical manifestations of the syndrome include obesity, dyslipidemia, hypertension, insulin resistance, and proinflammatory as well as prothrombotic states (27). The above confirmed increased risk of cholelithiasis in obese diabetics with hypertriglyceridemia may also be an indicator of its association with the metabolic syndrome (10, 26). Although the presence of some conflicting results in the literature (12-14), we did not find any significant association between cholelithiasis and smoking in the present study ($p > 0.05$). On the other hand, the lower prevalence of hyperbetalipoproteinemia in the cholelithiasis patients in the present study (9.7% versus 18.0%, $p < 0.05$), although the significantly higher mean BMI values of them, should be researched with further studies. As a conclusion, cholelithiasis is a common pathology in society and nearly four-fold more frequent in women, particularly in their fifties. There are significant relationships between cholelithiasis and parameters of the

metabolic syndrome including female predominance, elder age, BMI, obesity, hypertension, and hypertriglyceridemia. On the other hand, the significantly lower prevalence of hyperbetalipoproteinemia in the cholelithiasis patients should be researched with further studies.

References

- Eckel RH, Grundy SM, Zimmet PZ. The metabolic syndrome. *Lancet* 2005; 365: 1415-1428.
- Helvacı MR, Kaya H, Sevinc A, Camci C. Body weight and white coat hypertension. *Pak J Med Sci* 2009; 25: 6: 916-921.
- Helvacı MR, Aydin LY, Aydin Y. Digital clubbing may be an indicator of systemic atherosclerosis even at microvascular level. *HealthMED* 2012; 6: 3977-3981.
- Helvacı MR, Aydin Y, Gundogdu M. Atherosclerotic effects of smoking and excess weight. *J Obes Wt Loss Ther* 2012; 2: 7.
- Tazuma S. Gallstone disease: Epidemiology, pathogenesis, and classification of biliary stones (common bile duct and intrahepatic). *Best Pract Res Clin Gastroenterol* 2006; 20: 1075-1083.
- Katsika D, Grijbovski A, Einarsson C, Lammert F, Lichtenstein P, Marschall HU. Genetic and environmental influences on symptomatic gallstone disease: a Swedish study of 43,141 twin pairs. *Hepatology* 2005; 41: 1138-1143.
- Lammert F, Sauerbruch T. Mechanisms of disease: the genetic epidemiology of gallbladder stones. *Nat Clin Pract Gastroenterol Hepatol* 2005; 2: 423-433.
- Erlinger S. Gallstones in obesity and weight loss. *Eur J Gastroenterol Hepatol* 2000; 12: 1347-1352.
- Mathus-Vliegen EM, Van Ierland-Van Leeuwen ML, Terpstra A. Determinants of gallbladder kinetics in obesity. *Dig Dis Sci* 2004; 49: 9-16.
- Fraquelli M, Pagliarulo M, Colucci A, Paggi S, Conte D. Gallbladder motility in obesity, diabetes mellitus and coeliac disease. *Dig Liver Dis* 2003; 35: 12-16.
- Devesa F, Ferrando J, Caldente M, Borghol A, Moreno MJ, Nolasco A, et al. Cholelithiasis disease and associated factors in a Spanish population. *Dig Dis Sci* 2001; 46: 1424-1436.
- Kono S, Eguchi H, Honjo S, Todoroki I, Oda T, Shinchi K, et al. Cigarette smoking, alcohol use, and gallstone risk in Japanese men. *Digestion* 2002; 65: 177-183.
- Okamoto M, Yamagata Z, Takeda Y, Yoda Y, Kobayashi K, Fujino MA. The relationship between gallbladder disease and smoking and drinking habits in middle-aged Japanese. *J Gastroenterol* 2002; 37: 455-462.
- Jorgensen T. Gall stones in a Danish population. Relation to weight, physical activity, smoking, coffee consumption, and diabetes mellitus. *Gut* 1989; 30: 528-534.
- Bowman RL, DeLucia JL. Accuracy of self-reported weight: a meta-analysis. *Behav Ther* 1992; 23: 637-635.
- Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult

Treatment Panel III) final report. *Circulation* 2002; 106: 3143-3421.

17. O'Brien E, Asmar R, Beilin L, Imai Y, Mallion JM, Mancia G, et al. European Society of Hypertension recommendations for conventional, ambulatory and home blood pressure measurement. *J Hypertens* 2003; 21: 821-848.

18. Helvacı MR, Seyhanlı M. What a high prevalence of white coat hypertension in society! *Intern Med* 2006; 45: 671-674.

19. Funahashi T, Nakamura T, Shimomura I, Maeda K, Kuriyama H, Takahashi M, et al. Role of adipocytokines on the pathogenesis of atherosclerosis in visceral obesity. *Intern Med* 1999; 38: 202-206.

20. Widlansky ME, Gokce N, Keaney JF Jr, Vita JA. The clinical implications of endothelial dysfunction. *J Am Coll Cardiol* 2003; 42: 1149-1160.

21. Ridker PM. High-sensitivity C-reactive protein: Potential adjunct for global risk assessment in the primary prevention of cardiovascular disease. *Circulation* 2001; 103: 1813-1818.

22. Yudkin JS, Stehouwer CD, Emeis JJ, Coppel SW. C-reactive protein in healthy subjects: associations with obesity, insulin resistance, and endothelial dysfunction: a potential role for cytokines originating from adipose tissue? *Arterioscler Thromb Vasc Biol* 1999; 19: 972-978.

23. Zhou B, Wu Y, Yang J, Li Y, Zhang H, Zhao L. Overweight is an independent risk factor for cardiovascular disease in Chinese populations. *Obes Rev* 2002; 3: 147-156.

24. Zhou BF. Effect of body mass index on all-cause mortality and incidence of cardiovascular diseases--report for meta-analysis of prospective studies open optimal cut-off points of body mass index in Chinese adults. *Biomed Environ Sci* 2002; 15: 245-252.

25. Calle EE, Thun MJ, Petrelli JM, Rodriguez C, Heath CW Jr. Body-mass index and mortality in a prospective cohort of U.S. adults. *N Engl J Med* 1999; 341: 1097-1105.

26. Helvacı MR, Kaya H, Gundogdu M. Association of increased triglyceride levels in metabolic syndrome with coronary artery disease. *Pak J Med Sci* 2010; 26: 667-672.

27. Tonkin AM. The metabolic syndrome(s)? *Curr Atheroscler Rep* 2004; 6: 165-166.

SUMO1 pseudogene 3 (SUMO1P3) expression in human gastric cancer and its clinical significance

Hamid Reza Baradaran-Ghahfarokhi (1, 2)

Habib Malekpour (1, 2)

Ehsan Nazemalhosseini Mojarrad (2)

Hamid Asadzadeh Aghdaei (3)

Azar Baradaran (4)

Majid Asadi-Samani (5)

(1) Department of Biotechnology, School of Advanced Technologies in Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

(2) Gastroenterology and Liver Diseases Research Center, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran

(3) Basic and Molecular Epidemiology of Gastrointestinal Disorders Research Center, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran

(4) Department of Pathology, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran

(5) Student Research Committee, Shahrekord University of Medical Sciences, Shahrekord, Iran.

Correspondence:

Dr. Habib Malekpour

Shahid Beheshti University of Medical Sciences,

Taleghani Hospital, Evin,

Tehran, Iran,

Tel:+98 21 224 325 25

Fax:+98 21 224 325 17

Email: habib.malekpour@gmail.com

Abstract

Introduction/Aim: The aim of this study was to investigate SUMO (small ubiquitin-like modifier) 1 pseudogene 3, SUMO1P3 expression, as one of the pseudogene-expressed long non-coding RNA (lncRNAs) in gastric cancer (GC) patients.

Materials and Methods: Fresh gastric cancer and adjacent non-tumor tissues were collected from 182 GC patients, who were admitted to the Alzahra Hospital, Isfahan, Iran on December 2014 to January 2016. Quantitative reverse transcription-polymerase chain reaction was used to investigate the SUMO1P3 levels. Then, the association between the level of SUMO1P3 in gastric cancer tissues and the clinicopathological features of patients with gastric cancer was analyzed. To find the differences of SUMO1P3 levels between gastric cancer tissues and adjacent non-tumor tissues, one-way analysis of variance (ANOVA) was applied. A significance level of 0.05 was considered for the tests.

Results: The results showed that SUMO1P3 levels in males were not significantly higher than those in females ($p = 0.485$). No significant difference of SUMO1P3 expression was observed between patients under 64 years old and above ($p = 0.155$). The SUMO1P3 levels were not associated with perineural invasion ($p = 0.319$), lymphatic invasion ($p = 0.797$), invasion depth ($p = 0.790$), location of the tumor ($p = 0.811$), tumor size ($p = 0.635$), and grading ($p = 0.289$).

Conclusions: These results indicated that in our patient population and according to the used method in this study, pseudogene-expressed lncRNA SUMO1P3 may not be a potential biomarker in the diagnosis of gastric cancer.

Key words: SUMO1P3, long non-coding RNA, tumor marker, gastric cancer

Introduction

Gastric cancer (GC) is one of the most leading causes of cancer death nowadays and is considered as the most common gastrointestinal malignancy in some parts of the world, especially; East Asia, Eastern Europe, and parts of Central and South America (1-3). Nevertheless, since there are no specific symptoms for patients with early stage of GC, it is usually diagnosed at advanced stage and, accordingly, the prognosis for advanced stage GC is considerably poor for most of the patients (4, 5).

For GC prognostic prediction, there is still no commonly-accepted biomarker to facilitate the management of GC patients (2, 6). Therefore, detection of the new biomarkers for GC may play a significant role in improving diagnosis and also treatment of human GC. In addition, a detailed evaluation of the molecular mechanisms underlying gastric carcinogenesis can open new horizons for GC treatment.

Recent studies have shown that, large size long noncoding RNA (lncRNA) [size > 200 nt], is a new class of the noncoding RNA that contributes in cellular development, differentiation, and many other biological processes (7). Moreover, it has been stated that expression of lncRNA is associated with cancer development and progression (8, 9).

According to the recent reports, several types of lncRNAs have been detected and most of them have specific names (10, 11). Among the lncRNA family, the pseudogene-expressed lncRNAs are one of the major types. For this family, the 'P' suffix is used for pseudogenes of the both lncRNA classes and protein-coding genes. It should be noted that pseudogenes, considered as defunct relatives of functional genes, are nonfunctional genomic DNA sequences which are similar to normal genes. However, there is still very limited evidence of the clinical association between pseudogene expressed lncRNAs and GC.

The aim of this study was to investigate SUMO (small ubiquitin-like modifier) 1 pseudogene 3, SUMO1P3 expression, as one of the pseudogene-expressed lncRNAs in GC patients.

Materials and Methods

The study protocol was approved by the Ethical Committee of Shahid Beheshti University of Medical Sciences in accordance with standards set by the committee and in compliance with the 1975 Helsinki Declaration and its revision in 2000. Fresh gastric cancer and adjacent non-tumor tissues were collected from 182 GC patients, who were admitted to the Alzahra Hospital, Isfahan, Iran between December 2014 to January 2016. Before the study, patients gave their informed consent.

The study protocol was in accordance with Mei et al (6). After performing the biopsies, the specimens were immediately soaked in RNA-fixer Reagent (Exiqon, Helsinki, Denmark) and stored at -80 °C until performing the laboratory tests.

In this study, noncancerous tissues biopsies were taken from the adjacent tissues located 5 cm away from the edge of gastric cancer. An expert pathologist reviewed the samples and found the border where there were no obvious tumor cells.

For each sample, the total RNA was extracted using TRIzol reagent (Exiqon, Helsinki, Denmark) according to the instructions published by the manufacturer. Next, reverse transcription (RT) was performed using random primers and oligo(dT)15 primer in the GoScript RT System (Exiqon, Helsinki, Denmark).

For the polymerase chain reaction (PCR), the GoTaq qPCR master mix (Exiqon, Helsinki, Denmark) was used on the Mx3005P QPCR System (Corbet, Sydney, Australia). Similar to the other publications, the "b-Actin was amplified to normalize the relative levels of lncRNA". Sangon Biotech (Exiqon, Helsinki, Denmark) was used to synthesize the primers for SUMO1P3 and b-actin. Their sequences were as follows:

"50-ACTGGGAATGGAGGAAGA-30 (sense) and 50-TGAGAAAGGATTGAGGGAAAAG-30 (antisense) for SUMO 1P3; 50-AAGCCACCCCACTTCTCTCTAA-30 (sense) and 50-AATGCTATCACCTCCCCTGTGT-30 (antisense) for b-actin". The data were analyzed by the DcT method [8]. All results are expressed as the mean ± SD of three independent experiments.

Pathological characteristics of the patients including; perineural invasion, lymph metastasis, invasion depth, location of the tumor, tumor size, staging and grading were also recorded.

Histological grading was performed according to the National Comprehensive Cancer Network clinical practice guideline of oncology (V.1.2011).

Statistical analysis

To find the differences of SUMO1P3 levels between gastric cancer tissues and adjacent non-tumor tissues, one-way analysis of variance (ANOVA) was applied. The correlation between SUMO1P3 level and clinicopathological factors was further analyzed by ANOVA and t-test. Statistical analysis was performed using SPSS version 16.0 (Chicago, IL). A significance level of 0.05 was considered for the tests.

Results

Table 1, illustrates the SUMO1P3 expression levels and demographic characteristics of the patients including age and gender.

Table 2, shows the relationship between SUMO1P3 expression levels (Ct) in GC diagnosed patients.

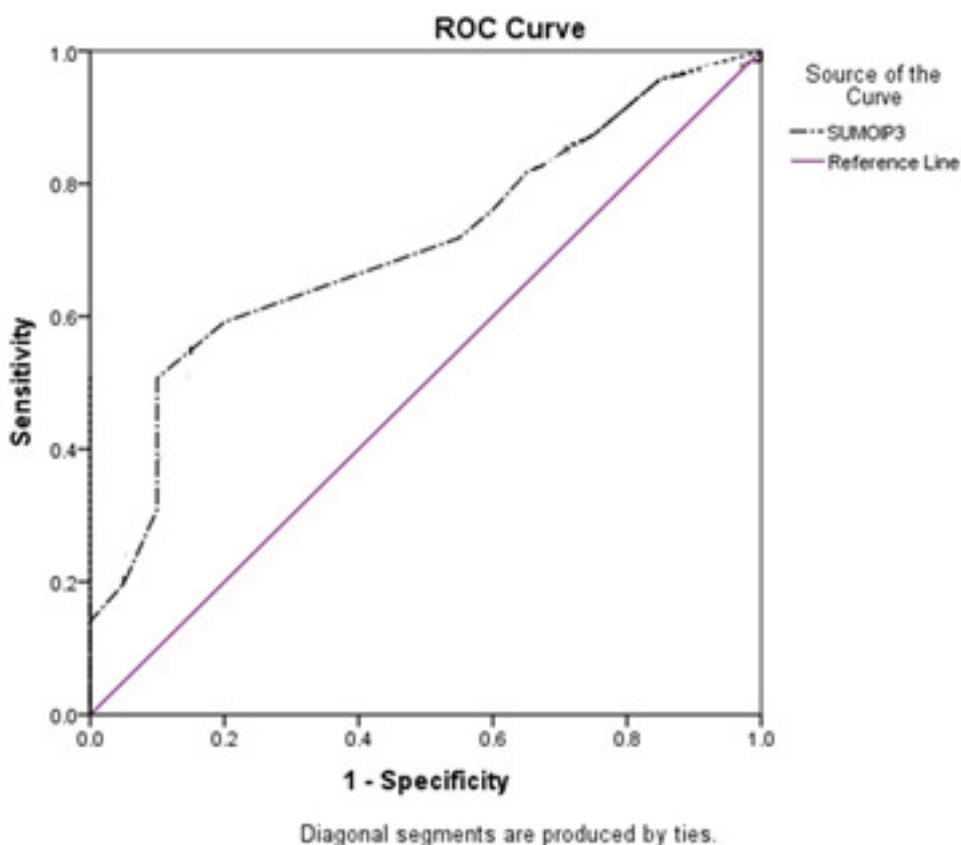
Figure 1, gives the ROC curve of the SUMO1P3 levels between gastric cancer tissues and adjacent non-tumor tissues.

Table 1: The SUMO1P3 expression levels and demographic characteristics of the patients including age and gender

P-value	Non-cancerous		Cancerous		Characteristics
	Percentage	Quantity	Percentage	Quantity	
0.001	70	28	39.4	56	< 64
	30	12	60.6	86	> 64
< 0.001	65	26	31	44	Female
	35	14	69	98	Male

Table 2: The relationship between SUMO1P3 expression levels (ΔC_t) in GC diagnosed patients

P-value	Non-cancerous		Cancerous		ΔC_t
	SD	Mean	SD	Mean	
0.005	2.8	-29.1	11.7	-23.6	SUMOIP3

Figure 1: The ROC curve of the SUMO1P3 levels between gastric cancer tissues and adjacent non-tumor tissues

The results showed that SUMO1P3 levels in males were not significantly higher than those in females ($p = 0.485$, Table 3). No significant difference of SUMO1P3 expression was observed between patients under 64 years old and above ($p = 0.155$, Table 3). In other words, patients below 64 years-old showed higher SUMO1P3 levels compared to those older than 64.

As shown in Table 3, the SUMO1P3 levels were not associated with perineural invasion ($p = 0.319$), lymphatic invasion ($p = 0.797$), invasion depth ($p = 0.790$), location of the tumor ($p = 0.811$), tumor size ($p = 0.635$), and grading ($p = 0.289$).

Table 3: The relationship between SUMO1P3 expression levels ($\Delta\Delta Ct$) and pathological factors among the studied patients

p value	Mean \pm SD	No. of patients (%)	Factors		
0.485	5.768 \pm 1.389	4 (40%)	< 64	Malignant	Age (year)
	5.2636 \pm 2.090	6 (60%)	\geq 64		
0.155	5.821 \pm 1.563	2 (20%)	Male	Malignant	Gender
	4.924 \pm 2.211	8 (80%)	Female		
0.319	5.150 \pm 2.029	6 (60%)	Positive		Perineural invasion
	6.086 \pm 1.473	4 (40%)	Negative		
0.797	5.408 \pm 2.083	6 (60%)	Positive		Lymph invasion
	5.375 \pm 1.696	4 (40%)	Negative		
-	5.434 \pm 2.048	10 (100%)	Positive		Lymph node metastasis
	-	-	-		
0.750	-	0 (0%)	T1-T2		Invasion depth
	5.323 \pm 1.971	10 (10%)	T3-T4		
0.811	5.429 \pm 2.066	10 (10%)	NON CARDIA		Location of the tumor
	-	0 (0%)	CARDIA		
0.625	5.095 \pm 0	2 (20%)	Small		Tumor size
	5.476 \pm 2.019	8 (80%)	Large		
-	-	0 (0%)	1-2		Staging
	5.566 \pm 2.068	10 (10%)	3-4		
0.289	5.196 \pm 0	2 (20%)	1		Grading
	-	0 (0%)	2		
	4.910 \pm 2.076	8 (80%)	3		

Discussion

In this study, we were interested in evaluating the expression of lncRNA SUMO1P3 at a molecular level as one of the pseudogene-expressed lncRNAs in GC patients.

Recent studies have shown that, lncRNA plays an important role in gastric cancer (9, 12). However, considering the pseudogene expressed lncRNAs, the potential of lncRNAs as a clinical diagnostic marker for clinical applications is still basically unknown.

Our results revealed that the expression levels of SUMO1P3, one of the transcripts of pseudogene, were not up-regulated in gastric cancer. As opposed to our findings, a recent publication by Mei et al (6). indicated that "pseudogenes might play their cancer-associated roles in RNA level".

We also followed different parameters affecting the SUMO1P3 expression in our patients including; age, gender, tumor size, differentiation, lymphatic metastasis, invasion (13, 14). No significant up-regulation of SUMO1P3 expression in our patients with GC was found for the mentioned factors (Table 3).

We found that SUMO1P3 expression is independent of age. This result was in agreement with previous reports, stating that some lncRNAs such as gastric-cancer-associated transcript 1, GACAT1, have been proved to be independent of age (9, 15, 16). It should be noted that, for some types of cancer, gender is concerned to be a factor to influence its incidence (9, 15, 16). In our study, we investigated that gender was not a factor that is significantly related to SUMO1P3 expression in patients with GC ($p = 0.485$, Table 3).

In the previously published papers, the relationship between invasion and lymphatic metastasis in GC and miRNA expression has been reported (17). Our results indicated a non-significant relationship between invasion and lymphatic metastasis in GC and lncRNA expression (Table 3).

In recent years, the understanding of GC biomarkers has undergone a marked change (1, 18-24). Descriptions of gastric wall function have evolved from an impermeable and passive barrier to a multifunctional tissue layer with an active role in dynamic cellular communication and adaptive permeability (1, 7, 25).

On the basis of the present results and according to the used method for our patient population, we can believe that lncRNA SUMO1P3 may not be a potential biomarker in the diagnosis of gastric cancer. However, more accurate follow-up studies are needed for the evaluation of the variations of lncRNA SUMO1P3 expression for gastric cancer patients. The results here should be confirmed in larger series, considering confounding factors (26, 27), and providing a more detailed assessment of lncRNA SUMO1P3 levels using other modalities.

Conclusions

In this work, expression of lncRNA SUMO1P3 in gastric cancer patients was evaluated. No statistical significant change of pseudogene-expressed lncRNA SUMO1P3 was seen according to the used method in this study. Therefore, pseudogene-expressed lncRNA SUMO1P3 may not be a potential biomarker in the diagnosis of gastric cancer.

Acknowledgements

This study was carried out as a PhD thesis by HBGh at Shahid Beheshti University of Medical Sciences, Tehran, Iran. We would like to thank the staff of Dr Baradaran Pathology Laboratory, Isfahan for their kind contribution to this study.

Conclusions

- Herszenyi L, Tulassay Z. Epidemiology of gastrointestinal and liver tumors. *European review for medical and pharmacological sciences*. 2010 Apr;14(4):249-58. PubMed PMID: 20496531.
- Zhang EB, Kong R, Yin DD, You LH, Sun M, Han L, et al. Long noncoding RNA ANRIL indicates a poor prognosis of gastric cancer and promotes tumor growth by epigenetically silencing of miR-99a/miR-449a. *Oncotarget*. 2014 Apr 30;5(8):2276-92. PubMed PMID: 24810364. Pubmed Central PMCID: 4039162.
- Shahbazi-Gahrouei D, Keshkar M. Magnetic nanoparticles and cancer treatment. *Immunopathol Persa*. 2016;2(1):e03.
- Catalano V, Labianca R, Beretta GD, Gatta G, de Braud F, Van Cutsem E. Gastric cancer. *Critical reviews in oncology/hematology*. 2009 Aug;71(2):127-64. PubMed PMID: 19230702.

- Morabito A, Carillio G, Longo R. Systemic treatment of gastric cancer. *Critical reviews in oncology/hematology*. 2009 Jun;70(3):216-34. PubMed PMID: 18829344.
- Mei D, Song H, Wang K, Lou Y, Sun W, Liu Z, et al. Up-regulation of SUMO1 pseudogene 3 (SUMO1P3) in gastric cancer and its clinical association. *Medical oncology*. 2013 Dec;30(4):709. PubMed PMID: 23996296.
- Li CH, Chen Y. Targeting long non-coding RNAs in cancers: progress and prospects. *The international journal of biochemistry & cell biology*. 2013 Aug;45(8):1895-910. PubMed PMID: 23748105.
- St Laurent G, Wahlestedt C, Kapranov P. The Landscape of long noncoding RNA classification. *Trends in genetics : TIG*. 2015 May;31(5):239-51. PubMed PMID: 25869999. Pubmed Central PMCID: 4417002.
- Sun W, Wu Y, Yu X, Liu Y, Song H, Xia T, et al. Decreased expression of long noncoding RNA AC096655.1-002 in gastric cancer and its clinical significance. *Tumour biology : the journal of the International Society for Oncodevelopmental Biology and Medicine*. 2013 Oct;34(5):2697-701. PubMed PMID: 23645148.
- Wright MW, Bruford EA. Naming 'junk': human non-protein coding RNA (ncRNA) gene nomenclature. *Human genomics*. 2011 Jan;5(2):90-8. PubMed PMID: 21296742. Pubmed Central PMCID: 3051107.
- Yin DD, Liu ZJ, Zhang E, Kong R, Zhang ZH, Guo RH. Decreased expression of long noncoding RNA MEG3 affects cell proliferation and predicts a poor prognosis in patients with colorectal cancer. *Tumour biology : the journal of the International Society for Oncodevelopmental Biology and Medicine*. 2015 Jun;36(6):4851-9. PubMed PMID: 25636452.
- Xiao B, Guo J. Long noncoding RNA AC096655.1-002 has been officially named as gastric cancer-associated transcript 1, GACAT1. *Tumour biology : the journal of the International Society for Oncodevelopmental Biology and Medicine*. 2013 Oct;34(5):3271. PubMed PMID: 23754450.
- Amiri M. On the occasion of world cancer day 2017; breast cancer. *J Prev Epidemiol*. 2017;2(2):e07.
- Rastegari F, Rafieian-Kopaei M. Antioxidant supplements and cancer. *Immunopathol Persa*. 2016;2(2):e14.
- Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. *CA: a cancer journal for clinicians*. 2011 Mar-Apr;61(2):69-90. PubMed PMID: 21296855.
- Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics, 2012. *CA: a cancer journal for clinicians*. 2015 Mar;65(2):87-108. PubMed PMID: 25651787.
- Zheng B, Liang L, Huang S, Zha R, Liu L, Jia D, et al. MicroRNA-409 suppresses tumour cell invasion and metastasis by directly targeting radixin in gastric cancers. *Oncogene*. 2012 Oct 18;31(42):4509-16. PubMed PMID: 22179828.
- Acharya P, Beckel J, Ruiz WG, Wang E, Rojas R, Birder L, et al. Distribution of the tight junction proteins ZO-1, occludin, and claudin-4, -8, and -12 in bladder

epithelium. *American journal of physiology Renal physiology*. 2004 Aug;287(2):F305-18. PubMed PMID: 15068973.

19. Al-Mamgani A, Heemsbergen WD, Peeters ST, Lebesque JV. Role of intensity-modulated radiotherapy in reducing toxicity in dose escalation for localized prostate cancer. *International journal of radiation oncology, biology, physics*. 2009 Mar 1;73(3):685-91. PubMed PMID: 18718725.

20. Ataman OU, Barrett A, Davidson S, De Haas-Kock D, Dische S, Dubray B, et al. Audit of effectiveness of routine follow-up clinics after radiotherapy for cancer: a report of the REACT working group of ESTRO. *Radiotherapy and oncology : journal of the European Society for Therapeutic Radiology and Oncology*. 2004 Nov;73(2):237-49. PubMed PMID: 15542172.

21. Budaus L, Bolla M, Bossi A, Cozzarini C, Crook J, Widmark A, et al. Functional outcomes and complications following radiation therapy for prostate cancer: a critical analysis of the literature. *European urology*. 2012 Jan;61(1):112-27. PubMed PMID: 22001105.

22. Amaral PP, Mattick JS. Noncoding RNA in development. *Mammalian genome : official journal of the International Mammalian Genome Society*. 2008 Aug;19(7-8):454-92. PubMed PMID: 18839252.

23. Chern CJ, Beutler E. Biochemical and electrophoretic studies of erythrocyte pyridoxine kinase in white and black Americans. *American journal of human genetics*. 1976 Jan;28(1):9-17. PubMed PMID: 2009. Pubmed Central PMCID: 1684914.

24. Fan Y, Wang YF, Su HF, Fang N, Zou C, Li WF, et al. Decreased expression of the long noncoding RNA LINC00261 indicate poor prognosis in gastric cancer and suppress gastric cancer metastasis by affecting the epithelial-mesenchymal transition. *Journal of hematology & oncology*. 2016 Jul 21;9(1):57. PubMed PMID: 27439973. Pubmed Central PMCID: 4955208.

25. Huang L, Xu A, Li T, Han W, Wu S, Wang Y. Detection of perioperative cancer antigen 72-4 in gastric juice pre- and post-distal gastrectomy and its significances. *Medical oncology*. 2013;30(3):651. PubMed PMID: 23820956.

26. Nikzad S, Mahmoudi G, Amini P, Baradaran-Ghahfarokhi M, Vahdat-Moaddab A, Sharafi SM, et al. Effects of radiofrequency radiation in the presence of gold nanoparticles for the treatment of renal cell carcinoma. *Journal of renal injury prevention*. 2017;6(2):103-8. PubMed PMID: 28497084. Pubmed Central PMCID: 5423275.

27. Nikzad S. The effect of intermittent radiotherapy on the cells' survival. *J Radiobiol*. 2015;2(1):11-5. doi: 0.15171/jrb.2015.03.

Decoy Cell Viruria in Kidney Transplant Patients. Does it correlate with Renal Function?

Akram Abedi (1)
 Mojgan Mortazavi (2)
 Omid Mirmosayyeb (3,4)
 Shahram Taheri (2)
 Nooshin Afsharmoghadam (1)
 Majid Asadi-Samani (5)
 Shahram Sajadieh (2)
 Azar Baradaran (1)

(1) Department of Pathology, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran

(2) Department of Nephrology, Isfahan Kidney Diseases Research Center, Isfahan University of Medical Sciences, Isfahan, Iran

(3) Department of Neurology, Isfahan Neurosciences Research Center, Al Zahra Hospital, Isfahan University of Medical Sciences, Isfahan, Iran

(4) Student Research Committee, Isfahan University of Medical Sciences, Isfahan, Iran

(5) Student Research Committee, Shahrekord University of Medical Sciences, Shahrekord, Iran

Correspondence:

Professor Azar Baradaran
 Department of Pathology,
 School of Medicine, Isfahan University of Medical Sciences,
 Isfahan, Iran

Email: azarbaradaran@med.mui.ac.ir

Abstract

Objective: BK virus (BKV) infection after kidney transplantation has been a topic of great interest in the recent decade. Prospective screening studies have revealed that BKVN is principally an early complication of renal transplantation occurring within the first post-transplant year in most cases. The aim of the present study was to observe the incidence of decoy cell viruria in renal transplant recipients. Furthermore, correlation of decoy cell viruria with graft function was assessed.

Methods: This analytic cross-sectional study was conducted in the Transplant Center of Alzahra Hospital, Isfahan, Iran between Jun 2014 and June 2015. Clinical screening for polyomavirus infection was done by means of urine cytological evaluation for decoy cells. Urine samples were analyzed in three steps including 2-4 months after transplantation, three and six months later.

Results: Thirty-three patients (22 male and 11 female) received kidney transplant from living donors. The average of patients' age was 41.9 ± 12.83 (range: 20-63 years). Peritoneal and hemodialysis

were used for 15.6% and 84.4% of recipients. The occurrence of decoy cell viruria at the time of enrollment, 3 and 6 months later was found in 18.2%, 10.7% and zero, respectively.

Conclusion: As urine cytology is easy to perform and of low cost, it is a useful tool for the investigation of active polyoma virus infection. Moreover, the findings advocate that the presence of decoy cells along with high creatinine is a better indicator of the virus presence.

Key words: BK Virus, Decoy Cell Viruria, Renal Transplantation, Renal Function

Introduction

BK virus (BKV) infection after kidney transplantation has been a topic of great interest in the recent decade. Human polyoma viruses are the members of the papova virus family which have a double strand DNA genome. The most identified species of this kind are BK-virus, JC-virus (JCV) and Simian-virus. BKV was first isolated from the urine of a renal transplant recipient with ureteric stenosis in 1971, but until 20 years later BKV was not recognized as a reason of interstitial nephritis and allograft failure in renal transplant patients. The preliminary infection may occur through fecal-oral transmission, respiratory tract and over the placenta. Also, they can be transmitted through organ transplantation. The vast majority of polyomavirus associated nephropathy (PVN) is triggered by the BKV, and the JCV is responsible for less than 3% of cases. (1)

BKV nephropathy (BKVN) which is involving 1-7% of renal transplant recipients, presented as a slow increase of serum creatinine. Prospective screening studies have revealed that BKVN is principally an early complication of renal transplantation occurring within the first post-transplant year in most cases. (2) Although the pathological view of tubulointerstitial nephritis can mimic rejection, the treatments for these two conditions are dissimilar: While dose reduction of immunosuppressant is the treatment of tubulointerstitial nephritis, treatment of rejection is by increase in immunosuppressant dose. (3)

As BKVN has restricted treatment options, the goal of screening is to facilitate primary diagnosis of patients when viruric or viremic, and to interfere before the development of overt nephropathy. After BK recurrence, the virus is first detectable in the urine, however, viremia develops after several weeks. Despite guidelines recommending quantitative polymerase chain reaction (PCR) for screening, urinary decoy cell detection is a potentially cost-effective alternative. (4) The aim of the present study was to observe the incidence of decoy cell viruria in renal transplant recipients. Furthermore, correlation of decoy cell viruria with graft function was assessed.

Methods and Materials

Recruiting patients

This analytic cross-sectional study was conducted in the Transplant Center of Alzahra hospital, Isfahan, Iran between Jun 2014 and June 2015. Ethical approval was attained from the local research ethics committee in school of medicine, Isfahan University of Isfahan before enrollment. (Approval code: IR.MUI.REC.1393.3030367, research project code: 393367) Informed written consent was obtained from all cases before recruiting in the study. Consecutive kidney transplant recipients from living donors who were older than 18 years were included. The inclusion criteria were to pass 1-4 months from transplantation. Patients who had a positive history of acute renal rejection or urothelial cancers were excluded. Also, patients were excluded from the study if they were unable to continue

due to any causes. In all patients a comprehensive questionnaire including recipient demographic features, past drug history, concomitant diseases, type and duration of dialysis and time after transplant were recorded.

Laboratory tests

Clinical screening for polyomavirus infection was done by means of urine cytological evaluation for decoy cells. Urine samples were analyzed in three steps including 2-4 months after transplantation, three and six months later. Early in the morning the patient voided the urine collected in the bladder overnight; the next fresh urine sample was referred to cytology laboratory within 15 minutes of micturition; 0.5-1 mL of urine was processed by liquid based cytology. Slides were immediately fixed in 95% alcohol for Papanicolaou staining. Time interval between the day of transplantation and first appearance of decoy cells in the urine and period of decoy cell persistence in the urine were assessed. Also, the number of decoy cells was counted in each smear. Qualitative urine and blood PCR for BKV DNA performed for patients were positive for presence of decoy cells in their urine cytology. Moreover, urine analysis was performed for all patients. Urine cytology was performed at 3 and 6 months after the first evaluation. Simultaneously, in order to assess renal function, serum creatinine was measured three times. Since GFR is considered as a highly sensitive and specific scale for chronic renal failure, it was calculated by MDRD formula based on serum creatinine. Transplant kidney biopsy was performed considering medical indications approved by expert nephrologist (5).

Statistical analysis

All data were analyzed using the SPSS®23 statistical software package. Quantitative demographic characteristics are expressed as mean \pm standard deviation (SD) and qualitative data are shown as a percentage. To compare means of two normally distributed data, the Student's t-test was used. For non-normally distributed data, the Mann-Whitney U-test was used. For comparisons of the correlations between the two groups, the chi-square and Fisher's exact tests were used. A p-value of <0.05 was considered statistically significant.

Results

Demographic data

Thirty-three patients (22 male and 11 female) received kidney transplant from living donors. The average of patients' age was 41.9 ± 12.83 (range: 20-63 years). Peritoneal and hemodialysis were used for 15.6% and 84.4% of recipients. After transplantation, patients received prednisone, cyclosporine, and mycophenolate mofetil. The average of months of interval between transplantation and the first assessment was 2 ± 0.9 months (range: 1-4). Demographic, clinical and para-clinical information of transplant recipients are revealed in Table 1.

Table 1: Demographic, Clinical & Paraclinical Information of Transplant Recipients Revealed

Patient demographic and lab data	Value
Age	41.9 ±12.83
Sex	
Male	66.7(%22)
Female	33.3 (%11)
Type of dialysis	
HD	81.8 (%27)
PD	15.5 (%5)
Non	3 (%1)
Duration on dialysis(month)	16.5 ±15.20
Months post transplantation	2.0 ±0.9
Last creatinine before sampling	1.31 ±0.24
Mena GFR	59.8±11.8
Cause of renal failure	
DM	24.2(%8)
HTN	21.2(%7)
GN	18.2(%6)
ADPKD	12.1(%4)
Others	24.2(%8)

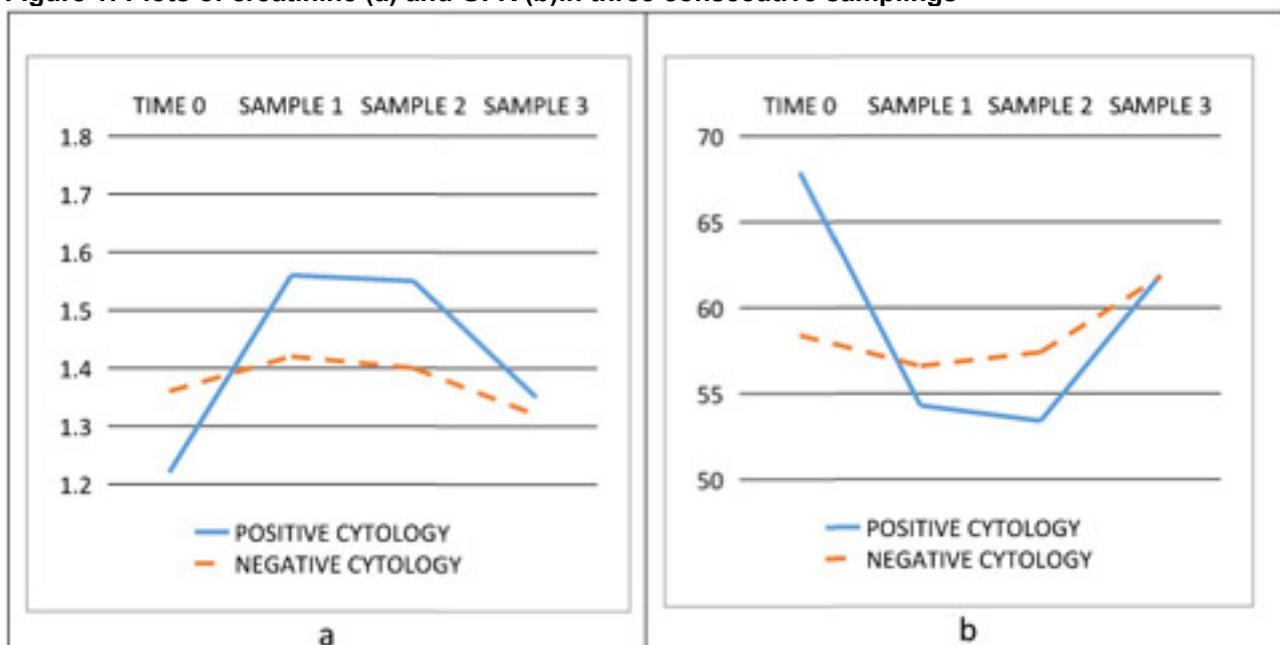
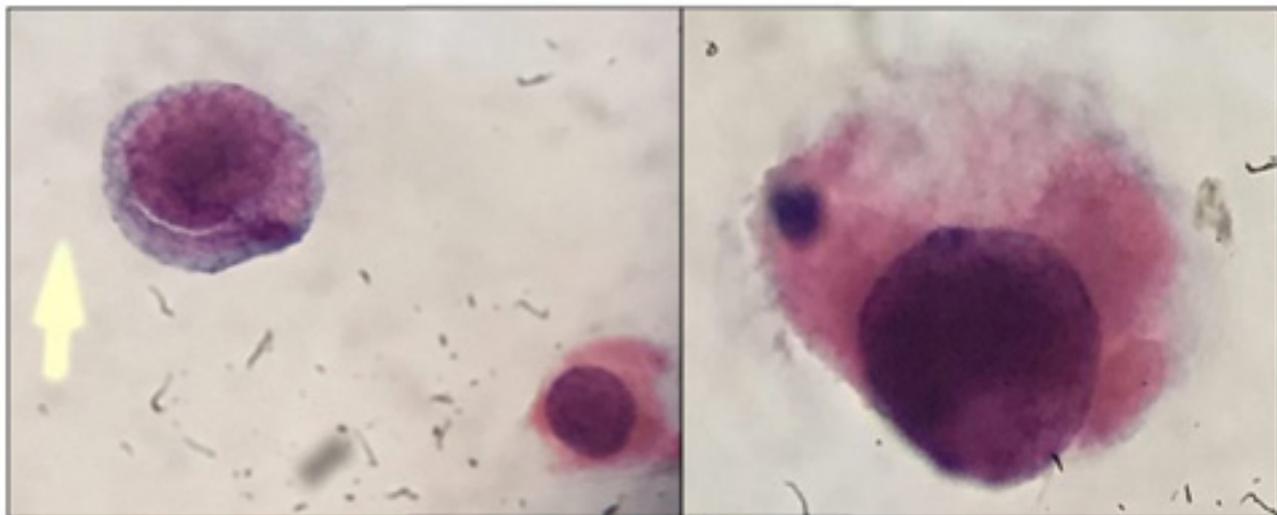
Figure 1: Plots of creatinine (a) and GFR (b) in three consecutive samplings

Table 2: Decoy Cell Per Smear

	1st step	2nd step	3rd step
Patient 1	4	6	0
Patient 2	15	0	0
Patient 3	3	3	0
Patient 4	13	12	0
Patient 5	3	0	0
Patient 6	1	0	0

Figure 2: Decoy cells with enlarged nucleus with a baso-philic intra-nuclear inclusion (papanicolaou stain *400)**Occurrence of decoy cell viruria**

Urine decoy cells were assessed in three mentioned intervals (at the time of enrollment, 3 and 6 months later). Definite presence of decoy cell, was proved by qualitative PCR of urine in all cases with positive sample (Figure 1). The occurrence of decoy cell viruria at the time of enrollment, 3 and 6 month later was found in 18.2%, 10.7% and zero, respectively. One case with decoy cell viruria and positive for CMV and BK-PCR underwent renal biopsy and showed no viral changes. The number of decoy cells in each high power field is shown in Table 1.

Evaluation of renal function

Serum creatinine and urine analysis were used for the evaluation of renal function. The level of creatinine was 1.43 ± 0.29 mg/dL, 1.39 ± 0.24 mg/dL and 1.35 ± 0.26 mg/dL in the three steps of the survey. Also, estimated GFR (eGFR) was calculated using the MDRD formula. In three steps of follow up the value of eGFR was 55.3 ± 11.4 mls/min/ $1.73m^2$, 57.3 ± 11.7 mls/min/ $1.73m^2$ and 61.8 ± 14.3 mls/min/ $1.73m^2$. The urinary WBC count was 8.0 ± 10.4 , 7.4 ± 4.1 and 6.7 ± 3.3 in three intervals. Moreover, the urinary count of RBC was 23.3 ± 17.7 , 9.2 ± 3.4 and 2.1 ± 1.6 respectively.

Correlation of decoy cell viruria and renal function

Independent t-test demonstrated that there is a significant difference between renal function and decoy cell viruria after 2 months of follow up. ($P= 0.017$) Moreover, the count of RBC was significantly lower in patients with decoy cell viruria ($P= 0.001$). After 5 months of follow up the level of creatinine was significantly higher in patients with decoy cell viruria (0.3 ± 0.17 vs 0.2 ± 0.04). Results of Spearman's rho test are demonstrated in Table 2. Regarding all of the 93 samples the level of creatinine was significantly higher in patients with decoy cell viruria. Additionally, there was no significant difference between occurrence of decoy cell viruria and count of WBC and RBC. In order to make a better correlation between decoy cell viruria and renal function, we divided patients into two groups, including GFR lower than 60 (group A) and larger and equal to 60 (group B). The average of patients' age in group A was significantly higher than group B (46.2 ± 11.5 vs 36.2 ± 12 , $P < 0.001$).

The GFR of groups A and B were 65 ± 13 and 56 ± 9 respectively and they were significantly different. Male patients were significantly more in group A rather than

females. 89% of patients with positive decoy cell viruria were in group A, while 60.2% of patients without decoy cell viruria were in this group ($P=0.039$). Since there was a significant correlation between post-transplantation GFR and age, sex and pre-transplantation GFR, we used logistic regression test to control their confounding effect. According to this, we concluded that there was a significant correlation between post-transplantation GFR and positivity for decoy cell viruria (OR=11.6; 95% CIs 1.12-120.04, $p=0.02$) (Figure 2).

Discussion

One of the leading causes of graft loss after kidney transplantation is polyomavirus. JC and BK virus infection is very prevalent in the first two years after transplant and might be monitored appropriately (6). Routine screening for BK has been shown to be effective in preventing allograft loss in patients with BK viruria or viremia. Reduction of immunosuppression remains the mainstay of BK nephropathy treatment and is the best studied intervention (7). The present study was conducted on thirty-three patients (22 males and 11 females) who received kidney transplantation from living donors. The average of patients' age was 41.9 ± 12.83 (range: 20-63) years. In a similar study in Iran thirty-one patients (21 men and 10 women) received kidney transplant from living donors. In this study, the average of patients' age was 38.3 ± 12.8 (range: 17-59) years (8). Urine cytology is a safe, noninvasive and sensitive tool for the evaluation and follow-up of renal transplant recipients and can be used as prospective screening for BKV allograft nephropathy (9). In BKV nephropathy, the finding of urinary decoy cells showed a 100% sensitivity, 84% specificity, 100% negative predictive value and 6% positive predictive value (10). In the first step of follow up of our study, the presence of decoy cells was 18.2% in kidney transplant recipients, while another report demonstrated the presence of decoy cells in 37.5% of patients (8). In this study, the occurrence of decoy cell viruria at the time of enrollment, and 3 and 6 months later was 18.2%, 10.7% and zero, respectively. Moreover, in another study the prevalence of polyoma virus infections increased with increasing time after transplantation (11), which is similar to the study by Liu et al. (12) Another same study revealed that Urinary decoy cell shedding was detected in 26.2% of 286 cases. BKV viruria was observed in 22.1% of 938 cases and BKV viremia in 5.2% of 1,029 cases. (13) One study in 2007, presented that significant polyoma viruses viruria is common following renal transplantation with onset usually within the first 3 months. Viruria is associated with worse graft function at 3 and 6 months. The time between urine positivity and clinical polyoma virus nephropathy is short. More frequent early urine screening would be required to achieve clinical benefit. In another study, the incidences of viruria and viremia at 1 year were 35% and 11.5%, respectively, compared with 17% and 3% at a time of 49 months post-transplantation. (10) Although managing a BKV infection includes reducing immunosuppression alone or combined with antiviral therapy, such as cidofovir or leflunomide, only an early diagnosis and reduction of immunosuppression reliably improve graft survival. (13)

The present study also revealed that the level of plasma creatinine was significantly higher in patients with decoy cell viruria. This correlation is similar to another study demonstrating that patients with BK-virus nephropathy had high serum creatinine that mimicked either tubular necrosis or rejection (14). The same study in 2006, suggested that the presence of decoy cells along with high creatinine is a better indicator of the virus presence. According to this study, there was a significant correlation between post-transplantation GFR and positivity for decoy cell viruria. Despite a low positive predictive value of decoy cells in urine, its absence has a negative predictive value of 100%, because almost all of those patients who did not have decoy cells had normal renal function.

Conclusion

In conclusion, our findings suggest that considering the risk of graft loss due to polyoma virus infection, routine urine cytology might be used as a screening method for the detection of polyoma virus infection. As urine cytology is easy to perform and of low cost, it is a useful tool for the investigation of active polyoma virus infection. Moreover, the findings advocate that the presence of decoy cells along with high creatinine is a better indicator of the virus presence (15).

References

1. Salvatore SP, Myers-Gurevitch PM, Chu S, Robinson BD, Dadhania D, Seshan SV. Polyoma (BK) virus associated urothelial carcinoma originating within a renal allograft five years following resolution of polyoma virus nephropathy. *Clinical nephrology*. 2016;85(3):179-83.
2. Esmaili H, Mostafidi E, Ardalan M, Vahedi A, Mahmoodpoor F, Mohajel-Shoja M. BK virus nephropathy is not always alone. *Journal of renal injury prevention*. 2016;5(1):12-6.
3. Petrov R, Elbahloul O, Gallichio MH, Stellrecht K, Conti DJ. Monthly screening for polyoma virus eliminates BK nephropathy and preserves renal function. *Surgical infections*. 2009;10(1):85-90.
4. Ghafari A, Lessan-Pezeshki M, Taghizadieh M, Rahimi E. BK polyoma virus nephropathy among Iranian renal transplant recipients. *Transplantation proceedings*. 2008;40(1):193-5.
5. Nesselhauf N, Strutt J, Bastani B. Evaluation of leflunomide for the treatment of BK viremia and biopsy proven BK nephropathy; a single center experience. *Journal of nephropathology*. 2016;5(1):34-7.
6. Taheri S, Kafilzadeh F, Shafa M, Yaran M, Mortazavi M, Seirafian S, et al. Comparison of polyomavirus (BK virus and JC viruses) viruria in renal transplant recipients with and without kidney dysfunction. *Journal of research in medical sciences : the official journal of Isfahan University of Medical Sciences*. 2011;16(7):916-22.
7. Koh MJ, Lim BJ, Noh S, Kim YH, Jeong HJ. Urinary decoy cell grading and its clinical implications. *Korean journal of pathology*. 2012;46(3):233-6.

8. Pezeshgi A, Ghods A, Keivani H, Asgari M, Shatty M. Incidence of BK Virus Nephropathy (BKVN) in Renal Transplant Recipients. *International journal of organ transplantation medicine*. 2012;3(3):115-8.
9. Jouve T, Rostaing L, Malvezzi P. Place of mTOR inhibitors in management of BKV infection after kidney transplantation. *Journal of nephropathology*. 2016;5(1):1-7.
10. Vidas Z, Misic M, Pacic A, Jurenec F, Knotek M, Kardum-Skelin I. The value of urinary decoy cells finding in patients with kidney transplantation. *Collegium antropologicum*. 2010;34(1):153-7.
11. Geramizadeh B, Roozbeh J, Malek-Hosseini SA, Azarpira N, Ayatollahi M, Salahi H, et al. Urine cytology as a useful screening method for polyoma virus nephropathy in renal transplant patients: a single-center experience. *Transplantation proceedings*. 2006;38(9):2923-5.
12. Liu LH, Fresco R, Picken MM. Pathologic quiz case. Intranuclear inclusions in allograft kidney. Pathologic diagnosis: human polyomavirus-associated interstitial nephritis in the allograft kidney. *Archives of pathology & laboratory medicine*. 2001;125(7):973-5.
13. Thamboo TP, Jeffery KJ, Friend PJ, Turner GD, Roberts IS. Urine cytology screening for polyoma virus infection following renal transplantation: the Oxford experience. *Journal of clinical pathology*. 2007;60(8):927-30.
14. Hirsch HH, Steiger J. Polyomavirus BK. *The Lancet Infectious diseases*. 2003;3(10):611-23.
15. Koshy PJ, Tripathy A, Vijayan M, Nair S, Yuvaraj A, Natarajan G, et al. A multicentre study of the spectrum of histopathological changes in renal allograft biopsies over a period of nine years from South India. *Immunopathol Persa*. 2017;3(1):e05.

To determine how frequently pregnant asthmatics are sensitive to food and inhalation allergens

Nasrin Fazel (1,2)

Michael Kundi (2)

Erika Jensen-Jarolim (3)

Isabella Maria Pali-Schöll (3)

Asghar Kazemzadeh (1)

Mojtaba Fattahi Abdizadeh (1)

Habibollah Esmaily (4)

Roya Akbarzadeh (1)

Raheleh Ahmadi (1)

(1) Sabzevar University of Medical Sciences, Sabzevar, Iran

(2) Center for Public Health, Medical University Vienna, Vienna, Austria,

(3) Institute for Pathophysiology and Allergy Research, Medical University Vienna, Vienna, Austria,

(4) Department of Biostatistics & Epidemiology, Neonatal Research Center, Mashhad University of Medical Sciences, Mashad, Iran

Correspondence:

Nasrin Fazel

Austria: Sollingergasse 8-12/9/2 ,1190 Wien

Iran: Pardis Sabzevar Medical university,

Sangsefid Road,

Sabyevar, Iran

Tel : +9851 44018300

Email: shohreh1368@yahoo.co.uk

Abstract

Background: Allergens are one of the causes of asthma attacks, i.e. an atypical immune reaction which is prompted by environmental allergens and mediated by IgE antibodies. The present study aims to identify the prevalence of inhalation and food allergens among pregnant Iranian women with asthma.

Methods: Euroimmun tests were performed to identify the prevalence of sensitivity towards allergens among pregnant asthmatics. A total of 1,603 women were selected from those who had visited Mobini Hospital in Iran August 2014-April 2015. We drew blood samples from these women and from cord blood, and postpartum, from their infants. These samples were used to measure IgE and RAST to inhalation and food allergens. Descriptive and comparative statistical analyses were performed.

Results: A total of 1,603 pregnant women referred to Mobini Hospital, Iran were included in the analysis. Thirty-four pregnant women were confirmed as having asthma. Women with asthma were significantly more often from villages ($p = 0.008$). There was a

statistically significant negative association between atopy and location as well as exercise-dependent wheezing ($p=0.048$, $p=0.004$, respectively). The seafood mix 3 was the most frequent allergen (10, 29.4%) detected in maternal blood samples, followed by peanut (6, 17.6%), and rough pigweed (5, 14.7%). All other allergens varied from 1 (2.9%) to 4 (11.8%). No association between IgE in maternal and neonate blood samples was detected.

Conclusion: Our results suggest that there is no transfer of sensitisation to selected inhalation and food allergens from mother to child. It may be important in future studies to try to detect local allergens that have the potential of such a transfer.

Key words: asthma, allergens, pregnancy, IgE

Introduction

In recent years, there has been a noticeable increase in the clinical and social burdens that accompany food allergies. Food reactions, when they involve the lung, tend to be severe, and therefore are important confounders in those with underlying asthma. Furthermore, food allergies also increase asthma morbidity, especially in early infancy; food allergy can be correlated to the expansion of future asthma. Diagnostic cut-off standards are very significant for specific IgE levels when interpreting food allergy. About 5% of asthmatics who react to food allergens suffer either an exacerbation of their asthma or a trigger of their current asthma, 6-8% of children and 2% of adults. (1) Moreover, edibles such as wheat, soya, peanut, milk and seafood may cause food-dependent exercise-induced anaphylaxis (FDEIA) (2). Whereas IgE specific to Ara h 2 has been shown to be diagnostic of peanut allergy, (3) recently, peanut lipid transfer protein has been described to be a significant allergen in the Mediterranean region.(4) Heterogeneous patterns of sensitization to individual peanut allergens are detected in different countries (5). The literature reported stronger pollution effects during the warm seasons, despite the culmination of pediatric asthma attacks during cold seasons. Sex and age differences may also confound the asthma effects from air contaminant exposure.(6) Peanut, wheat, and soy allergy were each cross-sectionally concomitant with increased childhood asthma, atopic dermatitis, and allergic rhinitis(7). Adhering to a healthy diet, including fruits, meat and fish, seems to ameliorate asthma and allergies during childhood. However, prospective and experimental studies are necessary to show a cause and effect relationship between diet and asthma / atopy. (8) A pollutant that can be easily verified by sampling serum levels is lead. Even so, the potential and severity of biological effects cannot be easily predicted (9). House dust mite (HDM) allergic rhinitis is difficult to diagnose, although numerous techniques are available (10). In humans, allergens from HDM, cockroaches, pets such as cats and dogs, pollen, and moulds have been recognized as the most relevant allergens (11). The prevalence of respiratory allergies is on the rise, among all populations, worldwide. Common symptoms of hypersensitivity include bronchial asthma, allergic rhinitis and atopic dermatitis. (12) Zicari's (2012) study confirms that early sensitization is an essential risk factor for the development of asthma. (13) Also, he stressed the importance of testing serum blood samples for aeroallergens. Because there are different numbers and types of allergens which vary according to country, many of which are absent in our area, it is necessary to do a variety of studies in order to identify most of the sensitized subjects, cost-effectively. Consequently, it will be useful to collect relevant causes of allergic diseases across various geographic areas, seasons, as well as environmental conditions. It might help with developing a new vision of the ideal environmental setting(s) in which to minimize atopy /asthma. Therefore, the aim of this study was to evaluate the prevalence of allergens identifiable by RAST test in pregnant asthmatics and their infants.

Method

A cross-sectional study was done on asthmatics whose diagnosis had been clinically confirmed by physical examination and pulmonary function test (PFT) among pregnant women who were referred to Mobini Hospital in Sabzevar between August 2014 and April 2015. The Ethics Committee of Sabzevar University approved the study protocol. The Radio-allergo-sorbent test (RAST) was done, using allergen extracts, to determine the patients' sensitivity to food and inhalation allergens. (20). RASTs were carried out using standardized allergen extracts for the following 36 aeroallergens and 36 food allergen: aspergillus fumigatus, cat, dog, cow, sheep, cage bird mix, sweet vernal grass, horse, *Alternaria alternata*, *Cladosporium herbarum*, pollens [tree (Ashe, Tree mixture), (Russian thistle,)], mites (*Dermatophagoides pteronyssinus*, *Dermatophagoides farine*), feathers mixture, cockroach peanut, seafood mix 3, banana, orchard grass, cultivated rye, alder, *penicillium notatum*, English plantain, goosefoot, rough pigweed, rice, grain mix 2, apple, cultivated oat, meadow foxtail, firebush, sorrel, tree mix 6, honeybee venom 1, house dust, cross-reactive carbohydrate determinants (CCD) marker, shrimp prawn, white pine, tree mix 4, rye flour, potato, rose, cultivated oat. From those mothers with clinically-confirmed asthma, in the final weeks of pregnancy, 7 cc of blood was drawn for total IgE and RAST. Additional blood samples from their neonates were obtained first day after delivery for the identical lab tests. The clot sample for allergens samples were transported to the laboratory quickly. Total serum was kept at -20° C until testing. Allergen samples for each series of experiments were stored at 4 ° C for up to 2 weeks, collected and tested. This methodology continued until all the required samples were gathered. Tests were performed using the ELISA kit (Euroimmun, Germany). In those patients with allergies to a wide variety of allergens, additional inhalation and food allergens were tested. Blood samples were processed in accordance with kit instructions, i.e. based upon the multiplex immunoblots method. Then the results of total serum IgE, using standard and allergens results, were evaluated with the software. Mothers were considered to be atopic if they had IgE \geq 160 kIU/L, infants if their serum IgE \geq 10 kIU/L. Any additional patient history was also recorded. The results were analysed using SPSS version 20.

Results

Cohort description

Out of 1603 pregnant women 34 (2.1%) had asthma. The majority of asthmatic patients were either 25-29 years (29 %) or \geq 35 years (35.3%) of age. The frequency of atopy in the study population of 34 asthmatic mothers and their infants was calculated as 7 (21%) and 4 (12%), respectively. Some allergens were much more common than others. (Tables 1, 2). Food allergy was defined as sensitization to at least 1 food allergen and was present in 28%. In a multivariate analysis, we found a significant relationship between prematurity and atopy or asthma ($P = 0.006$).

Allergies of pregnant women are related to asthma

To describe potential factors that might be connected to asthma during pregnancy (AP), we included the following parameters: eczema, allergies, asthma severity, asthma control, atopy, IgE, seafood mix 3 and rough pigweed. As controls, the same parameters were tested in the non-asthmatic mothers. The data were analysed using the chi-square statistic and Fischer's exact test. The highest rates of allergies were in the asthmatic group: 32 (94.1%) ($p = 0.001$). The majority of subjects in the asthmatic group did not have eczema, 30 (88.2 %). Asthmatic patients were divided into those with intermittent/mild persistent asthma (IMPA), and moderate or severe persistent asthma (MSPA). We found no significant relationship between atopy and asthma severity, with 22% and 14% atopy in IMPA and MSPA respectively. As well, there was no significant relationship between asthma control (i.e well-controlled, vs. partly/poorly-controlled) and atopy with 23% and 19% atopy, respectively. There was no association between atopy, and allergy or eczema (Fischer's exact test $p=0.37$ and $p=1.0$, respectively). There was also no significant statistical association between atopy and seafood mix 3 or rough pigweed, (both $p=1.0$) or any other allergen tested.

Hence, it appeared that only having allergy at pregnancy was closely linked to asthma, and it would be interesting to determine whether asthma might also be linked to additional health issues.

Atopy and location-dependent wheezing or exercise-induced wheezing of pregnant women are related.

To investigate whether further factors might also have contributed to AP, we tested the following factors: asthma severity, common allergens, smoker, passive smoker, atopy and infant gender.

There was a positive statistical association between atopy and location-dependent wheezing or exercise-induced wheezing, $p=0.048$ and $p=0.004$, respectively. There were no association between asthma severity and the most common allergen in asthmatic mothers, $p=0.71$ (Table 3). Table 4 shows the distribution of the variables retrieved from the databases for atopic women included in the study. There was no significant relationship between atopy and smoking or passive smoking $p=0.51$ and $p=0.58$, respectively. Taken together, it appeared that both allergy and atopy and location-dependent wheezing and exercise-induced wheezing in pregnant women were associated with a higher prevalence of asthma.

Table 1: Positive RAST results in cord and infant blood

Cord Blood	Number	Percent	Infant Blood	Number	Percent
Shrimp prawn	1	2.9	Rough pig weed	1	2.9
Seafood mix 3	1	2.9	Rose	1	2.9
Rough pig weed	1	2.9	Dermatophagoides d 1	1	2.9
Rose	1	2.9	Dermatophagoides d 2	1	2.9
Dermatophagoides d 1	1	2.9	Peanut	4	11.8
Dermatophagoides d 2	1	2.9	Cultivated oat	1	2.9
			English plantain	1	2.9
			Russian thistle	1	2.9

Table 2: Positive RAST results in pregnant women with asthma

Allergen	Number	Percent
Peanut	6	17.6
Seafood mix 3	10	29.4
Banana	3	8.8
Sweet vernal grass	2	5.9
Orchard grass	3	8.8
Cultivated rye	2	5.9
Alder	1	2.9
Penicillium notatum	1	2.9
English plantain	3	8.8
Cat	1	2.9
Goosefoot	4	11.8
Russian thistle	4	11.8
Rough pig weed	5	14.7
Rice	1	2.9
Grain mix 2	1	2.9
Apple	1	2.9
Cultivated oat	2	5.9
Meadow foxtail	1	2.9
Firebush	1	2.9
Sorrel	1	2.9
Tree mix 6	1	2.9
Honeybee venom 1	1	2.9
House dust	1	2.9
Dermatophagoides d1	1	2.9
Dermatophagoides d2	1	2.9
CCD marker	2	5.9
Ash	1	2.9
Shrimp prawn	1	2.9
White pine	1	2.9
Tree mix 4	1	2.9
Rye flour	1	2.9
Potato	1	2.9

Table 3: Frequency of positivity to seafood mix 3 in relation to asthma severity

Asthma severity	Seafood mix 3		Total
	negative	positive	
IMPA	19 (70%)	8 (30%)	27
MSPA	5 (71%)	2 (29%)	7

IMPA: intermittent asthma/mild persistent asthma; MSPA...moderate and severe persistent asthma

Table 4: Characteristics of pregnant women with asthma by atopy status

Characteristics		Nonatopic	Atopic	Test
		N. %	N. %	
Age	≤24	4 (14.8)	1 (14.3)	Chi-square test p=0.07
	25-29	6 (22.2)	4 (57.1)	
	30-34	5 (18.5)	2 (28.6)	
	≥35	12 (44.4)	0 (0.0)	
Ethnicity	Farsi	13 (48,1)	2 (28,6)	Fisher's exact test p=0.42
	Turk	14 (51,9)	5 (71,4)	
Education	Elementary school	11 (40.7)	1 (14.3)	Chi-square test p=0.17
	High school	14 (51.99)	4 (57.1)	
	College & university	2 (7.4)	2 (28.6)	
BMI	<19.8	5 (18.5)	2 (28.6)	Fisher's exact test p=0.61
	19.8-26	22 (81.5)	5 (71.4)	
Smoking	Yes	2 (7.4)	1 (14.3)	Fisher's exact test p=0.53
	No	25 (92.6)	6 (85.7)	
Past smoker	Yes	4 (14.8)	2 (28.6)	Fisher's exact test p=0.58
	No	23 (85.2)	5 (71.4)	
Husband smoker	Yes	1 (3,7)	2 (28,6)	Fisher's exact test p=1.0
	No	26 (96,3)	5 (71,4)	
Infant weight	< 2500mg	1 (3.7)	0 (0.0)	Fisher's exact test p=1.0
	≥ 2500mg	26 (96.3)	7 (100.0)	
Delivery method	Normal	13 (48.1)	3 (42.9)	Fisher's exact test p=1.0
	Cesarean	14 (51.9)	4 (57.1)	
Apgar 1	<7	2 (7.4)	0 (0.0)	Fisher's exact test p=1.0
	>7	25 (92.6)	7 (100.0)	
Wheezing at exercise	Yes	24 (89%)	2 (29%)	Fisher's exact test p=0.004
	No	3 (11%)	5 (71%)	
Wheezing in special places	Yes	25 (93%)	4 (57%)	Fisher's exact test p=0.048
	No	2 (7%)	3 (43%)	

Discussion

This study is the first in Sabzevar to assess the prevalence of asthma and allergic sensitization and its association with IgE factors in pregnant women with asthma. Sabzevar is a city in north-eastern Iran. The region is semi desert with hot and dry summers and is an agricultural center for grape and raisin farming. In the present study, we looked into the possible connection between asthma and allergens. We found a significant relationship between allergies and asthma as well as atopy and location-related and exercise-induced wheezing in pregnant women. Atopy and asthma severity, atopy and allergic sensitizations to various food and inhalation allergens were not statistically significantly related.

We observed that food allergens were more common than aeroallergens in both mothers and infants. The frequency of atopy in asthmatic mothers and their infants were 21% and 12%, respectively. Our results are similar to those of Nabavi (2013). (14) It is possible that there are relations between the in utero environment in asthmatic pregnancies and the development of asthma during childhood, independent of genetic factors. This is suggested by atopy in children, which was more frequently related to maternal asthma or IgE levels, rather than paternal asthma or IgE. (15) The study prospectively followed 181 AP, 62% of whom were classified as atopic. (16) Comert reported a prevalence of 32.2% atopic cases in his study (17). This difference as compared with the findings in the present study is probably due to climatic factors (12).

This study is the first report of sensitization to food allergens in our region. A high rate of sensitisation to pollens was established in earlier studies in our country. A study in Mashhad (18), Iran reported that weeds had the highest rate of sensitization, among which Russian thistle (*salsolakali*) was the most common in childhood. This result is similar to our results in infants but, probably due to the dry climate or different method of testing, it was not the most common. Whereas we used the RAST, they applied the skin prick test. Also, in Shiraz, the prevalence pattern of sensitisations to different types of pollens (e.g weed, grass, trees), as well as in Tehran and Karaj (12) (herbaceae I/III/III, sycamore, chenopodium, tree mix, grass, ash and cedar) was similar to our study. In the Comert (2014) study, the most prevalent allergen was *Phleumpratense* (19.3%), whereas in our study, it was seafood mix 3 (29.4%). (17) In our study, food allergens were the most common in mothers and grass and peanut allergens in infants. Herbal topography, climate and temperature could be responsible for the difference. (18) Our results were similar to most European countries in that three to four allergens were recognized in 95% of all sensitized subjects. (17) It is well-known that allergic patients are commonly co-sensitized against different allergen sources. Advancement in the field of allergen description by molecular biological techniques has now shown that sensitization against different allergen sources can be clarified as cross-reactivity of IgE antibodies with fundamentally and immunologically linked components existent on these allergen sources.

(12) A survey in Kerman indicated that allergies to food and airborne allergens differ depending on the nutritional and environmental settings. (19) The sensitization rates to grass pollen varies between 19.5% and 69.9% among European countries, and it is the most common allergen in Austria, Denmark, England, Greece, Poland, Switzerland and the Netherlands (17). In contrast in Comert's study, the prevalence of *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae* was also high 16.2% and 10.5%, respectively. The sensitization rates to *Dermatophagoides pteronyssinus* varied between 16.8% and 68.8% within European countries. Indeed, it is the most common allergen in Belgium, France, Italy and Portugal. In our results, the frequency was 2.9%. Two studies in Turkey reported the prevalence of sensitization to allergens from cats and dogs. There is a growing tendency towards pet ownership in our country (20, 21), so this may become a problem in the future. In Comert's study, the sensitization rates to *Alternaria*, *Aspergillus* and *Cladosporium* were 1.1%, 0.9% and 0.7%, respectively. In Europe (22), however, the rate of *Cladosporium* allergies was reported to be between 0% and 12.8%. The cockroach allergen would have been an important allergen to assess if we had been able to test all of the subjects against this allergen. Mert's study reported 74.22% cockroach sensitisations (17)

Whereas a study in Ahvaz found the most prevalent sensitizing mould was *C. acremonium* followed by *Penicillium* spp, we did not find that the infants were sensitized to these; although we tested them for *Penicillium* spp and *Aspergillus* allergen. (24) *Penicillium*, *aspergillus*, and basidiospores are some of the fungal species that are associated with asthma and atopy in children (25). We found only one such subject. Bunyavanich (2014) reported that exposure to wheat during early pregnancy was associated with reduced odds of mid-childhood allergy and asthma. Alterations in immune function have been proposed as a mechanism contributing to later development respiratory disease (26). Since we have only investigated neonates, the further development of this group is a matter of further study.

The group of 34 asthmatic patients tested with the 36 food and 36 aeroallergen panel were comparatively young which could overestimate the prevalence of allergen sensitivity. (17) Our findings suggest a negative relationship between location and exercise-related wheezing and atopy and a slightly positive association between atopy and maternal and passive smoking. We found no statistically significant associations between atopy and method of delivery, parity, number of gravidities, and abortions. However, Pistiner's (2008) findings suggest that cesarean delivery is associated with allergic rhinitis and atopy among children with a parental history of asthma or allergies. This likely differs from our study due to the alternative characteristics of the populations we each studied, as well as the duration of follow-up and definition of the outcomes. (23) The Mean (SD) age of our asthmatic patient group 30.97 ±6.36 versus 27.33 ±5.91 seems to be lower than in the Spanish study, i.e, 36.2 ±12.72 versus 30±15 years, respectively, which could account for the lower prevalence of atopic sensitization found in our study. Another possibility

may be that the Spanish study consisted mainly of patients with allergic rhinitis; with 37% of them having asthma. (17)

Our main limitation was the lack of lab tests in the control group. A smaller sample size in contrast to earlier studies was another weakness of our study.

Conclusion

According to the results and environmental condition in the area of our study, the most common regional allergens were food allergens such as seafood mix 3 and peanut that should be given more attention. It may be important in future studies to try to detect local allergens that have a potential of materno-fetal transfer. Acknowledgments

This work was approved by the ethics committee of the Medical University of Sabzevar, Iran (Medsab Rec.93.36). We thank the vice-chancellor of the Sabzevar university -Iran for financial support of this research .We thank the personnel of Mobini and Vaseei Hospitals for their cooperation. We also thank all the mothers who participated in the study.

References

- Ozol D, Mete E. Asthma and food allergy. Current opinion in pulmonary medicine. 2008;14(1):9-12.
- de Silva NR, Dasanayake WMDK, Karunatileke C, Malavige GN. Food dependant exercise induced anaphylaxis a retrospective study from 2 allergy clinics in Colombo, Sri Lanka. Allergy, Asthma & Clinical Immunology. 2015;11(1):1.
- Pedrosa M, Boyano-Martínez T, García-Ara C, Caballero T, Quirce S. Utility of specific IgE to Ara h 6 in peanut allergy diagnosis. Annals of Allergy, Asthma & Immunology. 2015;115 (2):108-12.
- Pedrosa M, Boyano-Martínez T, García-Ara MC, Caballero T, Quirce S. Peanut seed storage proteins are responsible for clinical reactivity in Spanish peanut?allergic children. Pediatric Allergy and Immunology. 2012;23(7):654-659.
- Ackerbauer D, Bublin M, Radauer C, et al. Component-resolved IgE profiles in Austrian patients with a convincing history of peanut allergy. International archives of allergy and immunology. 2015;166(1):13-24.
- Zheng X-y, Ding H, Jiang L-n, et al. Association between air pollutants and asthma emergency room visits and hospital admissions in time series studies: a systematic review and meta-analysis. PloS one. 2015;10(9):e0138146.
- Bunyavanich S, Rifas-Shiman SL, Platts-Mills TA, et al. Peanut, milk, and wheat intake during pregnancy is associated with reduced allergy and asthma in children. Journal of Allergy and Clinical Immunology. 2014;133(5):1373-1382.
- Saadeh D, Salameh P, Caillaud D, et al. Prevalence and association of asthma and allergic sensitization with dietary factors in schoolchildren: data from the french six cities study. BMC public health. 2015;15(1):1.
- Schwela D. Air pollution and health in urban areas. Reviews on environmental health. 2000; 15(1-2):13-42.
- de Blay F, Doyen V, Lutz C, et al. A new, faster, and safe nasal provocation test method for diagnosing mite allergic rhinitis. Annals of Allergy, Asthma & Immunology. 2015;115(5):385-390. e381.
- Kim H-J, Kang M-H, Park H-M. Common allergens of atopic dermatitis in dogs: comparative findings based on intradermal tests. Journal of veterinary science. 2011;12(3):287-290.
- Singh AB, Mathur C. An aerobiological perspective in allergy and asthma. Asia Pacific Allergy. 2012;2(3):210-222.
- Zicari A, Indinnimeo L, De Castro G, et al. Food allergy and the development of asthma symptoms. International journal of immunopathology and pharmacology. 2012;25(3):731-740.
- Nabavi M, Ghorbani R, Asadi AM, Faranoush M. Factors associated with cord blood IgE levels. Asian Pacific Journal of Allergy and Immunology. 2013;31(2):157.
- Murphy V, Gibson P, Smith R, Clifton V. Asthma during pregnancy: mechanisms and treatment implications. European Respiratory Journal. 2005;25(4):731-750.
- Stenius-Aarniala B, Piirilä P, Teramo K. Asthma and pregnancy: a prospective study of 198 pregnancies. Thorax. 1988;43(1):12-18.
- Comert S, Demir AU, Karakaya G, Kalyoncu AF. Minimum prick test panel for adult patients with asthma and rhinitis in Ankara, Turkey. Journal of Asthma. 2014;51(4):417-422.
- Behmanesh F, Shoja M, Khajedaluae M. Prevalence of aeroallergens in childhood asthma in Mashhad. Macedonian Journal of Medical Sciences. 2010;3(3):295-298.
- Fouladseresht H, Safiri S, Moqaddasi M, Razeghi MS, Bazargan N. Prevalence of food and airborne allergens in allergic patients in Kerman. Journal of Kermanshah University of Medical Sciences (J Kermanshah Univ Med Sci). 2014;18(4):234-241.
- Bostanci I, Türktas I, Türkyilmaz C. Sensitization to aeroallergens in Ankara, Turkey. Allergy. 1999;54:1332-1334.
- Fusun KA. Cockroach sensitivity in inner-city allergic patients in Turkey. Turkish Respiratory Journal. 2001;2(1):17-20.
- Heinzerling L, Burbach G, Edenharter G, et al. GA2LEN skin test study I: GA²LEN harmonization of skin prick testing: novel sensitization patterns for inhalant allergens in Europe. Allergy. 2009;64(10):1498-1506.
- Pistiner M, Gold DR, Abdulkarim H, Hoffman E, Celedón JC. Birth by cesarean section, allergic rhinitis, and allergic sensitization among children with a parental history of atopy. Journal of Allergy and Clinical Immunology. 2008;122(2):274-279.
- Yang H, Xun P, He K. Fish and fish oil intake in relation to risk of asthma: a systematic review and meta-analysis. PloS one. 2013;8(11):e80048.
- Wen HJ, Chiang TL, Lin SJ, Guo YL. Predicting risk for childhood asthma by pre?pregnancy, perinatal, and postnatal factors. Pediatric Allergy and Immunology. 2015;26(3):272-279.
- Hollams EM, De Klerk NH, Holt PG, Sly PD. Persistent effects of maternal smoking during pregnancy on lung function and asthma in adolescents. American journal of respiratory and critical care medicine. 2014;189(4):401-407.



THE MENA ACCESSIBILITY, REHABILITATION AND DISABILITY CONFERENCE

The MENA Accessibility, Rehabilitation and Disability Conference is an initiative dedicated to raise awareness for an inclusive and built environment focusing on improving the quality of life for people with disabilities and will be hosted on the 19 – 20 October 2017.

The conference theme “**Creating An Inclusive and Barrier-free Environment for Everybody**” offers a forum to promote an interactive dialogue and exchange of information, experiences and knowledge about accessibility standards, effective strategies on rehabilitation and disability matters, with a particular focus on Dubai vision as it aims to achieve a disability-friendly city by 2020. Dubai has played a significant role in creating accessibility standards in the MENA region – How are we doing now in terms of achieving this target?

The conference is a 2-day initiative that will feature interactive panel discussions, session presentations, case studies and unparalleled networking sessions and will have the opportunity to meet and connect with the government authorities, leading rehabilitative and industry experts, medical doctors, international and regional organisations, educators, accessibility and assistive technology solution providers.

BENEFITS OF ATTENDING

- ✓ Up to date leading industry regulations and developments in accessibility, disability and rehabilitation initiatives
- ✓ An initiative that offers a holistic approach from the psychosocial being of people with disabilities to integrating them in the community through inclusive education, healthcare, skills-training capacity building and enhancing employment opportunities.
- ✓ Find out the latest regulatory updates and investment opportunities for an accessible and inclusive Education, Healthcare, Employment, Technology and Tourism in the region
- ✓ A forum for best practices and to promote dialogue and exchange of information, experiences and knowledge about effective policies, strategies and programs to address disability in the region.
- ✓ Gain insights on the government’s initiatives for its future development planning in achieving Dubai Disability Strategy 2020
- ✓ Learn from 20+ industry experts with profound experience as they share detailed session presentations and their experiences in terms of advancing an inclusive educational system, non-discriminative workplace, disability friendly community and environment and a responsive and rehabilitative healthcare and government.
- ✓ Promoting the exchange of innovative ideas in advancement of new assistive, adaptive and rehabilitative technology and applications
- ✓ Unparalleled networking opportunities to learn from the leaders in the industry

For further information about the ARD-MENA Conference, please visit:

W: www.ardisabilitiesmena.com | E: info@worldarenagroup.com

Promoting Self-Directed Learning in Family Medicine Residency Program in Saudi Arabia

Mohammed H Doghether

Correspondence:

Dr. Mohammed H Doghether, MD
Family Medicine & Medical Education Consultant
Postgraduate Training Center
Ministry of Health
P.O.Box 90945,
Riyadh 11623
Kingdom of Saudi Arabia
Email: doghether@gmail.com

Abstract

This paper examined fostering self-directed learning (SDL) in a residency program in family medicine in Saudi Arabia. It investigated the most effective ways to help in appropriate application of Self-directed learning in the residency program. Learning is maximized when it is self-directed so that residents study material that is most relevant to them. Medical residents learn best when they learn according to their perceived needs and competency gaps (learner-centered needs and gaps) which are more beneficial than teacher-centered ones. Residents engage in self-directed learning by first identifying a clinical problem, then pursuing the learning task, next acquiring the new knowledge or skill, and finally practicing the new knowledge or skill. In this paper, I have described a curricular intervention that employs several educational and administrative modalities to foster the self-direction in learning in the family medicine training program in Saudi Arabia.

Key words: medical education, family medicine, residency program

Introduction

“The only man who is educated is the man who has learned how to learn” Carl Rogers 1983

Although much of training in family practice addresses the formal medical education, it is increasingly believed that this is analogous to the tip of iceberg, as it has been recognized that active engagement in self-planned learning is more effective than passive learning. The acquisition of self-directed learning or Self Direction in Learning (SDL) skills and the ability to keep up to date with development in medicine are learning outcomes about which there is a general agreement (1).

The Saudi Commission for health specialties (SCHS) is the certifying and accrediting body for family physicians and family medicine residency programs in Saudi Arabia.

Saudi Board in family medicine consists of a four year residency training program. The graduated family physician is expected to be competent in managing diseases, up-to date in terms of patient care, and be responsible for his lifelong learning in a world of rapidly changing and expanding knowledge about treatment and investigations (2). In an attempt to meet these challenges, the scientific board of family medicine in SCHS has decided to reform the residency program from the traditional didactic teaching methods, to a competency-based training program (2). One of the attractions of competency-based CB curricula for reformers in medical education is the potential to foster self-directed learning as a lifelong habit. As has been mentioned in studies (3), during implementation of the CB program, it inconsistencies were found in the interpretation of self-directed learning and its importance in the residency program. Instead of developing self-direction, students became overly dependent on teacher instruction. The shift in the conceptualization of self-directed learning in CB Learning is obvious. The program is in need of developing a conceptual framework to guide teachers and students.

The primary purpose of the framework is to ensure that the goal of self-directed learning, and its relationship to the other goals of the residency program, are understood and interpreted consistently, and in a way that is most likely to achieve all goals effectively (4).

This paper explains the theories and principles on which the framework, of the family medicine residency program (FMRP) in Saudi Arabia is based.

SDL theories and principles:

Self-directed learning has been identified as an important ability for medical graduates (4).

Malcolm Knowles established a definition of SDL that guided work in this area. That definition is:

A process in which individuals take the initiative, with or without the help of others, in diagnosing their learning needs, formulating goals, identifying human and material resources, and evaluating learning outcomes. (5).

This definition described learners as they move linearly through a series of steps to reach their learning goals.

Hammond and Collins developed in response to the growth of the concept of SDL a more structured definition:

A process in which learners take the initiative, with the support and collaboration of others, for increasing self-and-social-awareness; critically analyzing and reflecting on the situations; diagnosing their learning needs with

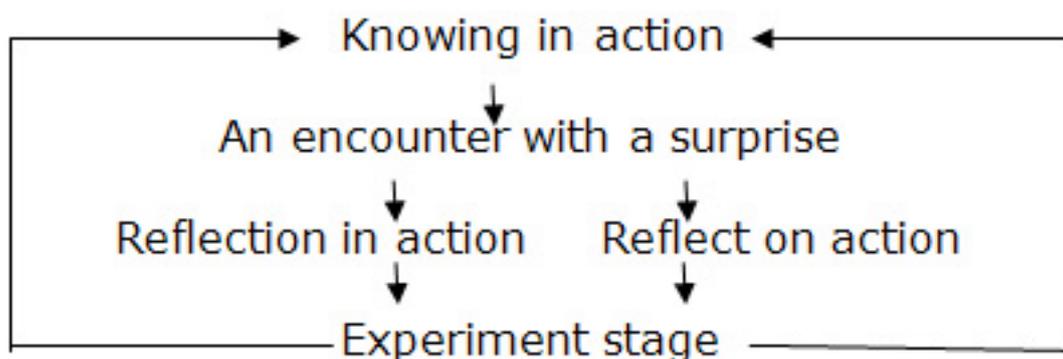
specific reference to competencies they have helped identify; formulating socially and personally relevant learning goals, identifying human and material resources for learning; choosing and implementing appropriate learning strategies, and reflecting on and evaluating their learning. (6).

This definition views the SDL process as more iterative, involving opportunities and interactions in the environment, the personality characteristics of learners, cognitive processes, the context of learning, and opportunities to validate and confirm SDL collaboratively. This definition forms the basis for more recent models in SDL e.g. the Personal Responsibility Orientation PRO by Hiemstra (7). In contrast to Self-directed learning; teacher-directed learning is learning where the teacher chooses what is to be learned, why it is to be learned, how it is to be learned, where, when, and at what level to be learned(4).

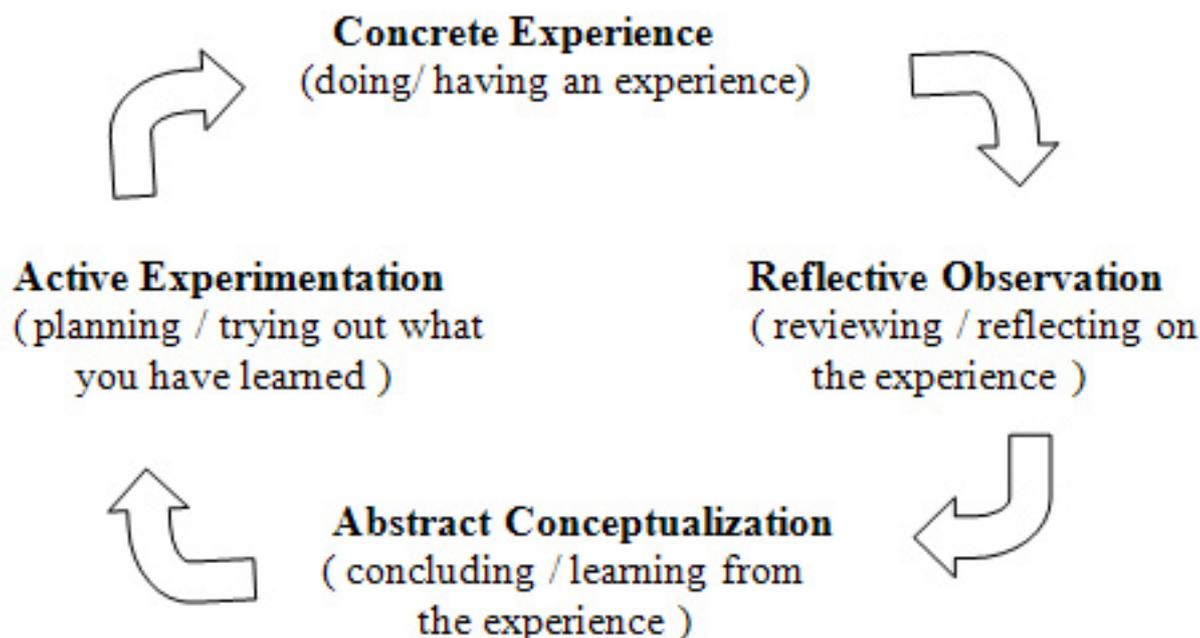
Among the bases for the self-directed learning theory is the ability to change in practice, which is known as reflective practice.

Reflective practice and learning from experience:

Patient centered education as well as learning from experience were the most important reasons as a basis for learning to change. Schon described a cycle of learning from experience that incorporates five stages (8, 9). An SDL approach is the most applicable when the learner already has some relevant knowledge and experience (4). While Kolb described a four stage learning process called the experiential learning theory (10).



Schon cycle of reflective practice-(Adapted from Prof Helen P Batty's lecture for Academic Fellowship Program in 2006).



Kolb's learning cycle

The strengths of SDL:

The strengths of SDL in the field of medical education are obvious; the following are summarized from several sources:

- Student-centered learning; where the student might not only choose what to study, but how and why that topic might be an interesting one to study. (11).
- Active learning; as adult learner, the student will be active in the process of learning where he will adopt deep approach to learning (12).
- Meets the needs of individual learners; learners have different needs and learn in different ways. SDL is an approach which encourages the learner's independency in the process of learning.
- Motivate the learner; as the learner becomes more independent, responsibility for his learning will be more; this in turn would increase his interest in the program and his motivation as a learner.
- Self-assessment; the learner will be encouraged to do self-assessment. Self-assessment by the learner will help him to recognize the gap in his knowledge and skills which will determine his learning needs.
- Self-learning skills; obviously SDL encourage not only mastery of the content area being studied but also the development of generic skills of self-learning. Learning how to learn is an important skill in continuing professional development (13).
- Constructivist approach-Students activate prior knowledge and build on existing conceptual knowledge frameworks (14).
- Outcome-based education; SDL is supported by outcome-based education (curriculum) which is considered more effective than process model of curriculum.
- Cost effectiveness; SDL provides coherent and effective learning strategy despite increasing student numbers. Enable educators to supervise larger numbers of learners.

Repetition of frequently taught materials can be avoided. Sharing of resources between institutions will reduce the need to duplicate resources. Saving time spent in formal education will support the role of educator as a learning facilitator.

The goal of self-directed learning in the postgraduate program:

Lifelong learning is the goal of Self-directed learning which Milflin (15) defined as the development of physicians who:

- Are conscious of the need and accept responsibility for evaluation of practice in the light of changing understanding.
- Are able to identify deficiencies or gaps in their own knowledge, skills and attitudes (KSA).
- Are motivated to generate a learning program to address deficiencies and fill the gaps in KSA, including finding and using the best evidence.
- Have the skills to identify, access and use resources wisely and efficiently;
- Are able to evaluate learning efforts, including resources used, and the effects on practice, and
- Are committed to repeating the cycle with each patient and clinical situation.

These skills meet the expectations of the SCHS which are the skills needed for a competent family physician.

Promoting SDL in residency program:

SDL is a comprehensive learning experience that includes well-defined objectives, pre- and post tests, and resources for accomplishing the objectives.

A model was developed to be a framework for understanding self-direction in adult learning; it consists of Personal Responsibility as a Central Concept, Self-Directed

Learning as The Process Orientation, Learner Self-Direction as The Personal Orientation, and Self-Direction in Learning as The Vital Link. This model was developed by Ralph G. Brockett and Roger Hiemstra(16), which they refer to as the “Personal Responsibility Orientation” (PRO) model of self-direction in adult learning (illustrated below) which is designed to recognize both the differences and similarities between self-directed learning as an instructional method and learner self-direction as a personality characteristic (7). This model is very interesting as it highlights the learner importance in the process of SDL.”The SDL as a process focuses on characteristics of the teaching-learning transaction. Thus, when considering this aspect of self-direction, concern revolves around factors external to the individual. Needs assessment, evaluation, learning resources, facilitator roles and skills, and independent study are a few of the concepts that fall within the domain of the self-directed learning process. The learner self-direction, centers on a learner’s desire or preference for assuming responsibility for learning. This is the personality aspect discussed earlier. Thus, self-direction in learning refers to both the external characteristics of an instructional process and the internal characteristics of the learner, where the individual assumes primary responsibility for a learning experience” (7). External factors and internal factors (personality characteristics) lie under the umbrella of the concept of Self Direction in Learning. “The PRO model illustrates this distinction between external and internal

forces. At the same time it recognizes, through the notion of personal responsibility, that there is a strong connection between self-directed learning and learner self-direction” (7).

Incorporating adult learning principles into a predesigned educational package is challenging. The solution might be through this model (PRO model);

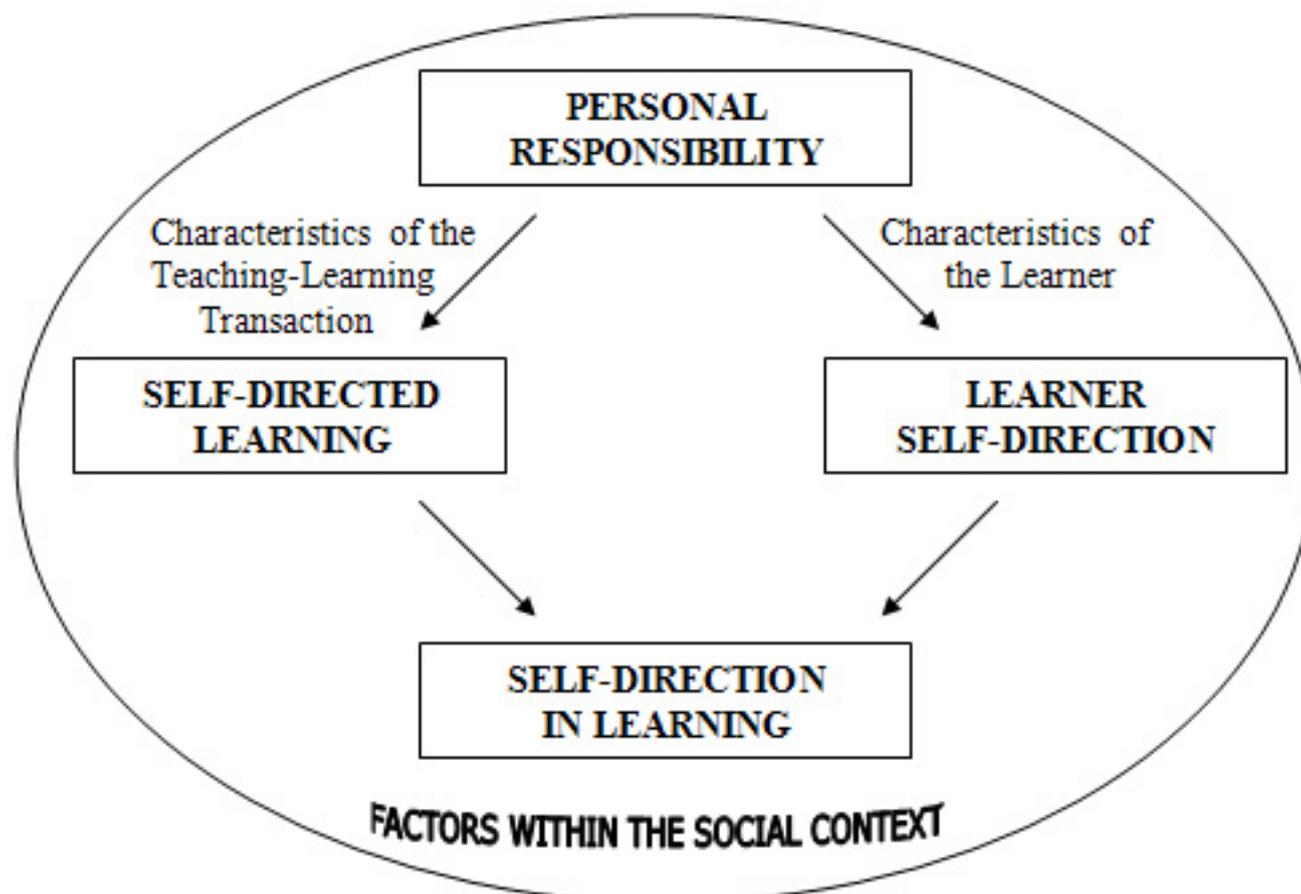
- I. learner self direction
- II. Self-directed learning as a process.

Learner self direction:

As mentioned above it deals with the personality characteristics of the learner that affect his survival in the self direction in learning.

Confidence is an essential component of SDL. Teaching that builds confidence, such as providing a supportive learning environment, supportive teacher attitude, acknowledgement of various learning styles and opportunities to practice new skills in a variety of settings will enhance the resident’s self-concept as a competent learner (17).

It is easiest when the learner already possesses skills that facilitate SDL such as self-assessment skills and library and informatics skills and other skills, which will be mentioned later.



The “Personal Responsibility Orientation” (PRO) Model. Reprinted with permission, Hiemstra, R. (7).

The SDL concept is somewhat not the usual strategy in the training programs in Saudi Arabia, where the learner has limited opportunities to assume control of the learning process. The learners in the training program need to develop fundamental skills. Learners in our program (FMRP) need to be trained in these skills:

- Self-assessment and identify their learning needs.
- Information searching for the health care literature and other databases
- Reading and critically appraising the medical literature
- Clinical decision-making skills

These skills are preferably to be posed in the early months of the program.

For the learners to develop these skills in SDL, they need an intensive facilitation and mentoring process by trained teachers. These processes should be applied to the new learners in the program (residents of first year R1).

Learners who are in advanced years might be enrolled with the new residents orientation to SDL skills if they are deficient in these skills, otherwise if they have gained these skills but are relatively inexperienced in SDL, they might benefit from orientation short courses.

An example is one-month rotation in which they learn informatics, critical appraisal, and clinical decision-making skills. Residents are required to apply these skills by critically assessing a clinical practice of their choice. At the end of the month, they formally present their findings to an invited audience. Time is provided within the curriculum for residents to work on their projects.

SDL as a process:

Discussion groups promote active participation in the learning process. Problem solving activities such as case studies help the learners to validate and use their experience as a learning source. Working in groups is also believed to decrease anxiety associated with lack of knowledge about the topic (4).

During the first year of implementation of the SDL in a PBL-curriculum, they found differences of opinion among staff and students, and between staff and students, about how to achieve the goal (1). When the concept of self-direction became counterproductive, dissonance about the concept caused difficulties in the implementation of the program. These difficulties might be dealt with by preparing both teachers and students to the process. Support to the student and teacher through attending workshops preparing them to identify their roles in the process of SDL would help to minimize the inconsistency among the educators and learners regarding the level of input they were willing to give in relation to SDL, which would be frustrating to both the student and the teacher (18).

Development of self-directed modules requires a substantial investment of time and work for the teachers. The immediacy of giving the learner an answer (pearls), spoon-feeding is

quick, but long term outcome is uncertain. Encouraging the learner to find the answers will have advantages of more student-teacher contact which will be reflected positively on their relationship and hopefully promote the process of SDL further in terms of implementation.

Role of the Mentor:

According to the Society of General Internal Medicine; mentoring is "a voluntary relationship in which the mentor is usually an experienced, highly regarded, empathetic individual, often working in the same organization, or field, as the mentee".

The Mentor role is significant as a contact to and guide for the learner to foster the SDL. Within the mentorship process, a mentor often assumes multiple roles (19). The mentor may be a role model, ensuring availability of resources, and to provide the Learner with constructive feedback. Mentor may be adviser, guide, listener, coach, friend, or facilitator. The role that best describes the mentor may be decided as a result of how well the mentor understands the total mentorship process. Clearly, the mentor role does not suit all people, including professors (20). This challenge needs us to train the mentors through frequent accredited workshops as part of continuing professional development CPD program for the teachers (trainers). These workshops must be SDL-based programs to help them learn and understand how to apply SDL.

Tools and resources used in evaluation of SDL:

Roger Hiemstra listed useful tools both for learner and educator to help in the self direction (see appendix B).

Difficulties in achieving the goal:

The ultimate result is the achievement of the goal of self-direction in learning, but some difficulties and barriers need to be addressed and dealt with.

An important thing is that adult learners do not always want to decide what to learn and how to learn in an unfamiliar environment. Self-directed learning may not be compatible with the learning styles of our learners; especially most of them lack the independent learning skills or have not been oriented on previous experience in undergraduate levels. The important result of the dissonance was that students become frustrated, struggling and many become dependent on direct educator guidance (asking educator to tell them what they would be assessed on).

As the learning is a change, and change may be threatening, the student and teacher need to feel secure and less threatened in the learning environment to the extent to dare to experience that which is new (20).

Lack of specific guidance and feedback to the student and teacher is one of the major reasons for the dissonance about the concept. This would lead to further frustration causing anxiety and distress for students. Feelings of frustration, anger and anxiety could affect motivation. The appropriate solution for this is through building a positive supportive student-facilitator relationship.

Monthly half-day tutorials will help the students to adopt the SDL in their learning where their concerns and worries may be addressed.

Follow up on what learner actually searched for, found, comprehended, and retained is often sporadic and unsystematic. This can be solved by educator assignments or learner's contract.

Challenges in the application of SDL:

The organizing committee for family medicine in the Saudi Commission of Health Specialties SCHS needs time and effort to recognize SDL model for learning and to adapt the process in the program in different training centres, thereafter to evaluate its application.

This SDL as a process needs training of the facilitators, mentors, students as well as teachers to adopt the SDL. Arrangement of workshops is costly to the individual training centers without the support of SCHS. Two large workshops per academic year per region (5 regions in Saudi Arabia) might be more practical than more frequent workshops.

As medical education is a new field in the country, the numbers of those who can help in preparation of the postgraduate training program to be SDL based program are limited. Asking the help of pioneers in this field from other countries might be appropriate at least in the first few years.

Although based on andragogical principles, the modules may be presented in a pedagogical way, thus promoting passive learning. The best way to master the rudiments of a new area is to be taught by an expert, at least at the beginning; introducing them to the fundamental principles and structures of SDL.

Self-directed modules may not be the best way to address learning needs in all domains of learning such as affective domain (4). Educators need to behave ethically, which includes not recommending a self-directed learning approach if it is not congruent with the learners' needs.

Students become better self-directed learners because of being in the curriculum for a longer time, and, hence, becoming more experienced. (15), which is an opportunity in our 4-years program.

Mifflin and his colleagues (15) published in the next year to their previous study on application of PB curriculum in undergraduate medical school that in the light of the literature of higher education and in the experiences of others in problem-based medical curricula, the Learners need support and guidance to foster the development of self-directed, lifelong learning. Publishing a guide for students to SDL, in which the general educational principles are explained, enables students to understand the nature and purpose of the self direction in learning as a model. This can be introduced in a thorough introduction to the curriculum by means of orientation programs.

The roles of the teacher/preceptor in SDL:

Students will be assessed formatively over time to ensure their development of skills to take greater responsibility for directing their own learning (21) including the foundation knowledge, reasoning skills and confidence (15).

Mifflin (15) described the tutor in SDL process as:

initially model, then coach, and, as students develop expertise in the process, the tutor fades, intervening only where appropriate to ensure students make optimal use of the case for learning, and to ensure that they continue to monitor the quality of learning.

In developing guidelines for educators, certain points need to be addressed. The following list summarizes points made by several writers (17) regarding how adult educators can best facilitate self-directed learning:

- Consider the student as an adult learner; with the background as the traditional teacher-centered learning as the student may be expected to have pitfalls in their understanding of the SDL and this needs to be addressed in the guidance.
- Help the learner identify the starting point for a learning project as it is new concept for them.
- Help learners acquire the needs assessment techniques necessary to discover what objectives they should set.
- Learn and teach inquiry skills, decision making, personal development, and self-evaluation of work.
- Promote gradual independence of the student.
- Encourage the setting of objectives that can be met in several ways and offer a variety of options for evidence of successful performance.
- Develop a partnership with the student by negotiating a learning contract for objectives, methods, and evaluation criteria.
- Make sure that learners are aware of resources and how to make use of them.
- Be a manager of the learning experience rather than an information provider.
- Provide examples of previously acceptable work (the minimal required). This will help in relieving student's anxiety.
- Recognize learner personality types and learning styles.
- Use techniques such as field experience and problem solving that take advantage of adults' rich experience base.

Role of educational institutions and employers:

The implementation of SDL will not be possible and maintained without the involvement of educational institutions and employers in providing SDL experiences. Hiemstra R (7) recommends certain points, the following:

- Conduct research on trends and learners' interests.
- Obtain the necessary tools to assess learners' current performance and to evaluate their expected performance.
- Provide opportunities for learners to reflect on what they are learning through half-day tutorial every week.

- Encourage critical thinking skills by incorporating such activities as seminars.
- Create an atmosphere of openness and trust to promote better performance.

I would add these points to what Hiemstra mentioned above:

- Promote Problem based small group learning.
- Promote inter-professional learning and teaching.
- Have the program directors meet regularly with panels of experts who can suggest curricula and evaluation criteria.
- Help protect learners against manipulation by promoting a code of ethics.
- Provide educators training on SDL.
- Provide a consult office for both educators and students for the best ways to deal with obstacles in application of SDL
- Conduct a 4 years-cyclical evaluation of the program process and outcome.

Resources

Blended learning, defined as the combination of traditional face-to-face learning and asynchronous or synchronous e-learning. Blended learning appears to have a consistent positive effect in comparison with no intervention in health professions (22).

All students should have access to the training program Intranet and to the World Wide Web (23). Resources specific to training program needs are better provided in computer-based format (e-blackboard) to allow time-independent access for learners. Teachers should always be available through the bulletin board on the intranet website and by email. Those who are free can consult with educator on an individual basis if necessary.

Later in the program, learners rely less on educator-generated resources and use their patients as primary resources for learning. Although educators are encouraged to orient learners to resources in clinical departments, the educator is increasingly a role model and demonstrator of clinical practice rather than provider of factual knowledge and resources (15).

Information skills

By the availability of resources mentioned above, I believe that the first year learners need to make use of the training program liaison with information specialists (librarians) who need to spend considerable time coaching learners in accessing and using databases, both in conventional and electronic forms. In clinical rotations in years 3 and 4, learners should maintain proficiency by applying their information skills in evidence-based practice. Their access to and use of information sources is increasingly self-directed, encouraged by and modeled on the practice of their educators.

Methods used to foster SDL:

The following methods have been mentioned in literature as a practical tips for self direction in learning which are good to be used to foster the implementation of SDL in our program:

Targeting learner-specific needs. The claim that there is never enough time to teach everything about a clinical case, especially in outpatient teaching is no longer valid with one minute perception (OMP) as the teacher can know what is the learner's greatest need or deficit on a particular case. OMP is very helpful and perceived by residents as a good tool in family medicine teaching sessions (24).

Assignments. This is where a clinical question is identified during routine patient care by either the teacher or the student. The teacher will ask the student, or group of students to find related information that help in answering the question and report back to the teacher, group, or a class.

These assignments need to increase as the student becomes more familiar with information gathering skills.

Volunteerism: A day per week will be assigned for volunteerism where student or group of students independently identify a common need and search the answers which will help to adapt the reflective practice. This might be fostered further when the teacher can be a role model and practices some reflective practice in the teaching session with the students.

Dissemination of knowledge: As a result of the above two methods, I find dissemination of knowledge by and among the students will foster implementation of SDL. This can be achieved by student medical journal recognized by SCHS where publication in this journal is considered extra credit to the students.

Learning contracts LC: the first step in developing a positive student-teacher relationship is when a student and teacher agree, at the beginning of a rotation, on particular learning goals and come up with a plan for monitoring and evaluating progress. Students need help from the teacher on how to develop a LC. One day workshop for the teachers' refreshment on LC might be needed in the beginning of SDL implementation. (25)

As the LC is a dynamic in its nature, changing as the learner progresses in the learning process, the student will fill the LC with the help of the teacher and mentor, where it will be reviewed every three months for the 1st two years (R1 and R2), to adopt changes as the students progress in the program, then every year for the 2nd two years (R3 and R4).

Reporting back. Students will periodically (at every quarter of the rotation) report back to the teacher what they found. This is through a written format (log book, brief outline or 1-page handout, etc.). In this method the students will be asked to report back. It facilitates evaluation of the learner,

and requires the learner to critique, integrate, and present information. Feedback from the site of the teacher is important to help student improvement.

Resources: Where does the learner find information and answers? The program will offer standard textbooks, library electronic access (for medical literatures), electronic black boards or e-learning software platform like moodle e-learning platform (MEP) which enables educators to create online courses to encourage interaction and collaborative construction of learning content. It provides several opportunities for the 'teacher' to transform from being 'the source of knowledge' to being a facilitator and role model in the process of acquiring knowledge and skills (26).

As computers become more universally incorporated into clinic workstations, they will, in all probability, become the predominant resource.

Portfolios: A portfolio is a collection of products prepared by the student that provides evidence of learning and achievement related to a learning plan. A portfolio typically contains written documents but can include video or audio-recordings, photographs, and other forms of information. Students will be instructed to reflect upon what has been learned as this is an important part of constructing a portfolio. In addition to products of learning, the portfolio can include statements about what has been learned, its application, and remaining learning needs (27). Mentor would help student in identifying remaining learning needs and how they can be met. Portfolio will include a log of clinical procedures performed during training program; a summary of the research literature reviewed when selecting a treatment option; a quality improvement project plan (e.g. Audit project), and report of results; ethical dilemmas faced and how they were handled; a computer program that tracks patient care outcomes; or a recording or transcript of counseling provided to patients. Portfolio can be a paper work or electronic. The electronic one is very easy to design and practice with a lot of editing features, which I have practiced in the U of T e-blackboard.

Portfolios will be used for both formative and summative evaluation of students. Portfolios will be used for evaluating mastery of competencies that are difficult to evaluate in other ways such as practice-based improvement, use of scientific evidence in patient care, professional behaviors, and patient advocacy. Teaching experiences, morning report, patient rounds, individualized study or research projects are examples of learning experiences that portfolios will be most useful to assess them. The Royal College of Physicians and Surgeons of Canada in the Maintenance of Competence Program (MOCOMPS) has developed a portfolio system for recertification using Internet-based diaries called PCDiary© that could be adapted to residency evaluations (28).

Practice based small group learning: the evidence is supporting the use of Practice-Based Learning (PBL) as an effective method for teaching under-graduates in medical schools and used more and more in Continuous

Professional Development (CPD) activities (29). The research proves the PBSGL effectiveness in postgraduate teaching. (30, 31)

Conclusion

In the adult learning theory, adults learn best when they are required to address problems and learning is maximized when it is self-directed so that adults study material that is most relevant to them. Clinicians engage in self-directed learning by first identifying a clinical problem, then pursuing the learning task, next acquiring the new knowledge or skill, and finally practicing the new knowledge or skill.(32)

In this paper, I have described a curricular intervention that employs several educational and administrative modalities to foster the self direction in learning in family medicine training program in Saudi Arabia. The program should be designed to incorporate principles of adult-learning theory. The program should contain exercises to enhance skills for assessing learning needs, developing flexible short- and long-term learning plans, and asking and answering clinical questions efficiently. I sought to characterize the effects of this teaching program on physicians' self-reported learning behaviors and self-efficacy for performing essential self-directed learning behaviors. Appropriate support at appropriate intervals means that, over time, students are motivated and enabled to guide their own efforts, secure in the knowledge that they have developed the skills and attributes which will allow them to continue learning which is effective.

Increasingly, instructional methods (PBL, SDL, EBM) are viewed as complementary rather than exclusive models. Didactic and teacher-centered teaching probably still has a role, even as other instructional strategies are utilized. "Blended" teaching strategies rather than predominant teaching strategies are increasingly being promulgated.

References

- 1) Schostaka J, Davisb M, Jacky Hansonc J, Schostakd J, Browne T,Starkeg PD, Jenkinsh N. The Effectiveness of Continuing Professional Development. A report prepared on behalf of College of Emergency Medicine, Federation of Royal Colleges of Physicians and Manchester Metropolitan University, 2010.
- 2) Saudi Commission for Health Specialization SCHS (2016).Saudi Board for Family Medicine-Manual for training in family medicine. Retrieved November 3 ,2016, <http://scfhs.info/Issues/>
- 3) Abu Zuhairah A, Al-Dawood K, Khamis A. Family medicine training in Saudi Arabia: Are there any variations among different regions?. *Med Edu.* 2015; (22);2: 106-110.
- 4) Murad MH, Varkey P . Self-directed Learning in Health Professions Education . *Ann Acad Med Singapore.*2008;37:580-90
- 5) Knowles MS. *Self-Directed Learning .A guide for learners and teachers.* New York, NY: Associated Press;1975.

- 6) Hammond M and Collins R. Self-Directed Learning; Critical Practice. 1991, reprinted 2004. RoutledgeFalmer ISBN 0-7494-0299-7.
- 7) Hiemstra, R. Lifelong learning: An exploration of adult and continuing education within a setting of lifelong learning needs (Chapter 7 Theoretical bases and research in adult education) (Third Edition). Fayetteville, NY: HiTree Press; 2002. Retrieved November 3, 2016, <http://www-distance.syr.edu/llch7.html>
- 8) Schon D. The reflective practitioner. 1983; New York, NY: Basic Books.
- 9) Schon D. Educating the reflective practitioner. 1987; San Francisco, Calif: Jossey-Bass Publishers.
- 10) Kolb DA. Experiential Learning: Experience as a source of learning and Development. Englewood Calif, NJ: Prentice-Hall; 1984.
- 11) O'Neill, G., Moore, S., McMullin, B. Dublin: AISHE, Emerging Issues in the Practice of University Learning and Teaching.. Released under Creative Commons licence: Attribution-NonCommercial .2005; 2.0. Some rights reserved. <http://www.aishe.org/readings/2005-1/>
- 12) MacLeod N. "The 7 Benefits of Self-Directed Learning" Published on August 11, 2015 <https://www.linkedin.com/pulse/7-benefits-self-directed-learning-nancy-macleod>.
- 13) Harden, R. M. A new vision for distance learning and continuing medical education. *Journal of Continuing Education in the Health Professions* .2005;25: 43-51
- 14) Wood Diana F. ABC of learning and teaching in medicine: Problem based learning. *BMJ* 2003;326:328-330.
- 15) Mifflin BM, Campbell CB, Price DA. A conceptual framework to guide the development of self-directed, lifelong learning in problem-based medical curricula. *Med Educ*.2000;34:299-306.
- 16) Brockett R G and Hiemstra R . Self-Direction in Adult Learning: Perspectives on Theory, Research, and Practice. London and New York: Routledge; 1991. Available on the internet; <http://home.twcny.rr.com/hiemstra/sdindex.html>.
- 17) Guglielmino, L.M. The case of promoting self-directed learning in formal educational institutions. *SA-eDUC JOURNAL* 2013;(10): 2.
- 18) Lunyk-Child, O., Crooks D., Ellis P., Ofosu C., O'Mara L., Rideout E. "Self-directed learning: faculty and student perceptions", *J Nurs Edu*. 2001;40(3): 116-123.
- 19) Van Schaik S, Plant J, and O'Sullivan P. Promoting self-directed learning through portfolios in undergraduate medical education: The mentors' perspective. *2012; Medical Teacher*, 35(2).
- 20) Ali PA, Panther W . Professional development and the role of mentorship. *Nurs Standard*.2008 ;22(42): 35-39.
- 21) Dolmans HJM, Schmidt HG . What drives the student in problem-based learning? *Med Educ*.1994;28:372-80.
- 22) Bamidis P . The Effectiveness of Blended Learning in Health Professions: Systematic Review and Meta-Analysis. *J Med Internet Res* .2016; 18(1): e2.
- 23) Den Harder A, Frijlingh M, Ravesloot C, Oosterbaan AE, and van der Gijp A. The Importance of Human-Computer Interaction in Radiology E-learning . *J Digit Imaging*. 2016; 29(2): 195-205.
- 24) Moin M, Sadia S, Naqi S. STUDENT PERSPECTIVE ABOUT ONE MINUTE PRECEPTORSHIP IN A BUSY OUTPATIENT SETTING . *Pak Armed Forces Med J*. 2016; 66 (1):162-66
- 25) Robles J. Student Learning Contracts: Considerations for Implementation in Pharmacy Experiential Experiences. *J Pharma Care Health Sys* .2015;2: 135. doi:10.4172/2376-0419.1000135
- 26) Amandu GM, Muliira JK, Fronda DC. Using moodle e-learning platform to foster student self-directed learning: Experiences with utilization of the software in undergraduate nursing courses in a Middle Eastern university . *Procedia - Social and Behavioral Sciences*. 2013; (93): 677 - 683.
- 27) Challis M .AMEE medical education guide no. 11 (revised): Portfolio-based learning and assessment in medical education. *Med Teach*. 1999; 21: 370-86.
- 28) Toolbox of Assessment Methods, Version 1.1. Accreditation Council for Graduate Medical Education (ACGME), & American Board of Medical Specialties (ABMS).2000; Available online: <http://www.acgme.org/Outcome/assess/Toolbox.pdf>
- 29) Dent, J.A., Harden, R.M. A practical guide for medical teachers. Elsevier, Second Edition, chapters 7 and 16. 2005.
- 30) Cunningham D, McCalister P and MacVicar R . Practice-based small group learning: what are the motivations to become and continue as a facilitator? A qualitative study . *Quality in Primary Care*. 2011;19:5-12
- 31) Mazmanian P. and Feldman M. Theory is needed to improve education, assessment and policy in self-directed learning. *Medical education*. 2011;45(4), 324-6.
- 32) Carr L . Seven Preceptor Microskills: Pearls for More Effective & Efficient Clinical Teaching. Published on November 26, 2015 <https://www.linkedin.com/pulse/7-preceptor-microskills-pearls-more-effective-linda-carr-ph-d-?trk=mp-reader-card>

Appendices

A. LEARNING CONTRACTS

In developing your learning contract, it may be useful if you have a sense of your own learning and cognitive styles. The following figure is provided to facilitate the learner who has never filled out a learning contract in obtaining some sense of what might be the best approach for this course.

SOME GUIDELINES FOR THE USE OF LEARNING CONTRACTS (Murad MH, 2008).

How do you develop a learning contract?

- Step 1: Diagnose your learning needs.
- Step 2: Specify your learning objectives.
- Step 3: Specify learning resources and strategies.
- Step 4: Specify target dates for completion.
- Step 5: Specify evidence of accomplishment.
- Step 6: Specify how the evidence will be validated.
- Step 7: Review your contract with consultants.
- Step 8: Carry out the contract.
- Step 9: Evaluation of your learning.

Your Learning Style Preferences		
	Self-Directed Learner	Other-Directed Learner
Learner Dependent	Standard contract with suggested structure used as basic guide	Standard contract using instructor suggestions
Learner Independent	Create own contract in terms of content and procedure	Develop own version of contract using instructor suggestions

B. Types of Tools and resources used in SDL ((Murad MH, 2008).

Types of Tools and resources used in SDL	Tools and resources used for learner	Tools and resources used for tutor
Planning Tools	<ul style="list-style-type: none"> • The Learning Contract • Self Analysis as a Learner • Self-Directed Learning Readiness Scale • Self-Directed Learning Perception Scale (SDLPS) 	<ul style="list-style-type: none"> • Determining Your Teaching Style • Determining Individual Learning and Change Styles.
Individual Study Techniques	<ul style="list-style-type: none"> • Using Probes in Learning. • How to Read a Journal • Learning with Computers. • Using Self-Paced Modules. • Using Communication Technology. • Self-Directed Learning Modules. • Learning from Your Experiences. • Improving Writing Skills. 	<ul style="list-style-type: none"> • Using Communication Technology. • Self-Directed Learning Modules.
Personal Reflection Tools	<ul style="list-style-type: none"> • Book/Article/Media Review Techniques • Reflecting on Learning at the Workplace 	<ul style="list-style-type: none"> • Book/Article/Media Review Techniques
Individual Skill Development	<ul style="list-style-type: none"> • Portfolio Development • Improving Your Writing Skills • Improving your Discussing Skills, • Enhancing Your Questioning Skills, 	<ul style="list-style-type: none"> • Portfolio Development • Enhancing Your Lecturing Skills • Enhancing Your Coaching Skills

Gum *Sisymbrium irio* effect on the quality attributes of baguettes

Leila Azadi
 Mohammad Hojjatoleslamy
 Hooman Molavi

Department of Food science and technology,
 Islamic Azad University,
 Shahre Kord Branch,
 Shahre Kord,
 Iran

Correspondence:

Leila Azadi, Mohammad Hojjatoleslamy
 Department of Food science and technology,
 Islamic Azad University,
 Shahre Kord Branch,
 Shahre Kord,
 Iran

Email: mohojjat@iaushk.ac.ir

Abstract

In this study, gum *Sisymbrium irio* at different levels of Control, 1/0, 1/5 and 2/0 percent (w, w) and wheat flour, in loaf bread and its impact on the quality attributes including technological features, colours and staling throughout the day, and various storage mechanisms were evaluated. The results of the evaluation of technical features, showed that gum *Sisymbrium irio* increased humidity, reduced stiffness and reduced volume compared with the control bread. By increasing the hold time, stale bread and buns control treated with different levels of gum *Sisymbrium irio* significantly increased, shelf life.

Key words: Gum *Sisymbrium irio*, loaf bread staling, colorimetric

Introduction

In multi-phase systems such as bread dough, stable, hydroxypropyl methyl cellulose emulsion is maintained during baking. The hydrocolloid films, the phase boundary between gas bubbles, are created and provide stability of cells in the gas expansion and other changes in the process. When the temperature rises during baking, hydroxyl propyl methyl cellulose, hydrocolloid gels formed through the interaction of the chain and create a temporary network. This will boost the dough during the expansion and reduction in volume is prevented. The gel also acts as a barrier against loss of moisture and flavor without any adverse effect on soft tissue of bread (Appelqvist et al. 1997, Armero et al .1997). The type and amount of hydrocolloids in bread depends on the type of bread and also properties of the flour used. Usually hydrocolloids are used in loaf bread for tissue recovery, and to strengthen the gluten network, creating a smooth, uniform consistency and to delay staling. Carboxy methyl cellulose (CMC) with an average size is more consistent with the gum flour and has been added to the dough in along with other components such as sugar, so more water is absorbed. Some types of carboxy methyl cellulose have very good water holding capacity but relatively poor solubility, Water holding capacity in bakery products is very important. Carboxymethyl cellulose in food, increase efficiency, to delay staling and also increase product acceptance by consumers and increase shelf life, Carboxy methyl cellulose is compatible with other ingredients and bread improvers (Bell, DA. 1990). Effect of a combination of carboxymethyl cellulose and hydroxyl propyl cellulose with other additives such as enzymes and emulsifiers to check and confirm that the addition of carboxymethyl cellulose and hydroxyl propyl

cellulose improves the rheological properties of dough and bread shelf life (Sarkar et al.. 1995). Xanthan gum and Locust, studies about the impact on the quality of bread and colleagues show that this hydrocolloids, stale bread delay and increased moisture in the bread crumb has a positive impact on the stability of the dough and the final product. Meat product is used to increase the storage period (Collar.1996). In relation to the effect of adding gum on the rheological properties and breadmaking quality of the research was done and it was found that gum production to the dough, improves dough stability during fermentation and specific volume, water activity increased bread moisture is better preserved (Brady et al .1985, Selomulyo et al. 2007). In the study several hydrocolloids with different chemical structures in loaf bread were observed and that some of these hydrocolloids are able to a degree prevent loss of moisture during storage and speed dehydration of bread crumb reducing and preventing staling of bread. According to various researchers, hydrocolloids to conserve water and to prevent redistribution of bread, as well as preserving more [brain] volume and softness gas improves speed and reduces fresh bread staling. Hydrocolloids in bakery products can be used as fat replacers. Hydrocolloids, xanthan and tragacanth effect on the levels of 0/5 and 1/5 on the rheological and sensory properties of frozen dough from flour as a way to improve the quality of structural damage caused by freezing and frozen dough bread waste reduction and tails, were studied. Effect of guar gum, pectin, alginate, and xanthan Kapakaragynan looked on wheat flour paste features and was also studied. They use Mylugraf which showed that the addition of the hydrocolloids in quantities of 5/0% and 1% (w w) improves the properties of dough produced (Kim et al . 1977). The use of frozen dough bread is one way of effectively reducing the rate of bread staling. In this study, the effect of hydrocolloids, xanthan and tragacanth at two levels: 5/0 and 5/1 percent (w weight based on flour) on the rheological properties of dough and hamburger buns made from frozen dough stored (at oC18- for 2 weeks) and sensory quality were studied. The results of the study of several hydrocolloid with chemical structures from different loaf bread showed that some of these hydrocolloids are capable of loss of moisture during storage of bread and speed dehydration bread crumb, reduce the staling prevent (Guarda et al , 2004 , MacRitchie et al- . 1973). The results of Rojas and colleagues showed that the forming properties of wheat starch paste greatly improved by adding hydrocolloids. In addition, in several studies of gum as a fat replacer, is used to replace gluten and source of dietary fiber (Appelqvist et al. 1997). Effect of hydrocolloids alginate, xanthan and hydroxy propyl methyl cellulose the rheological properties of dough and bread quality, were examined. The results showed that the addition of these substances increases during fermentation dough stability and increased specific volume and holding., Also, adding the hydrocolloids reduces the hardness of the bread crumbing (Selomulyo et al . 2007). They found that all hydrocolloids are able to hold moisture loss during crumbing of bread and reduce the rate of water loss and moisture to increase the bread crumb (Guarda et al , 2004).

Methods

In this study, *Sisymbrium irio* Golestan Mohammadi was purchased from flour factories. The use of dry yeast factory production FARIMAN Mashhad. In Tables 1 and 2, respectively *Sisymbrium irio* characteristics of flour and gum used is listed.

Gum prepared *Sisymbrium irio*

Sisymbrium irio was 40 ° C for 4 hours in the water, after passing through the filter, the material after drying (gum) was added to breads and cakes.

Baking bread

Bread baguette in the bread industry unit according to Lee, who, has been mentioned in Table 3, were produced. After sieve weighing the dry ingredients for making bread they can be mixed together. The yeast suspension in water with a temperature of 35 ° C containing 5.0% sucrose for 10 minutes to activate the yeast cells was prepared, and was added to the above materials. Finally, the remaining water was also added to the formulation. All compounds were mixed at 1 mixer for 10 minutes. Pulp obtained from the following 4 treatment groups were prepared so that all of their components except *Sisymbrium irio* gum, were considered constant.

Treatment 1: No gum *Sisymbrium irio*

Treatment 2: containing 1.0% gum *Sisymbrium irio*

Treatment 3: 15/0 percent gum containing *Sisymbrium irio*

Treatment 4: 2.0% gum containing *Sisymbrium irio*

90 gram pulp were split into pieces and shaped in the form, respectively. Templates in the fermentation chamber temperature and relative humidity of 85% C ° 38 were placed for 60 minutes. Action Bake for 25 to 30 minutes at a temperature C ° 240 industries in the oven with steam injection was performed. After baking, breads were extracted from the mold, and cooled at room temperature for half an hour and then were packed in polypropylene bags until tests were kept at the right temperature.

Statistical analysis

Statistical tests based on completely randomized design with three treatments and three replications. First, by analyzing the variance in the comparison test Duncan means of a significance level of 5% was conducted to evaluate the significance of the results. Statistical analysis using Excel software and SPSS version 21 was conducted.

Table 1: Wheat and Flour Quality Characteristics in terms of dry matter

Test Method	Test result	Description of test
Iranian National Standard No. 2705	15/2	Humidity
Iranian National Standard No. 2863	12/14	Protein
	28/8	Gluten
Iranian National Standard No. 103	6/67	pH

Results and Discussion

Table 2, shows that the control samples had the sample had the highest humidity and low moisture content in the sample was found to contain 1.0 per cent Gum *Sisymbrium irio*. Eskandari and his colleagues, as well as Yarmand and Ardebil's similar results were reported (Yarmand et al . 2005, Poursmaeil. 2010). Russell et al., Guarda and colleagues and Poursmaeel also had similar results from adding hydrocolloids, xanthan gum, sodium alginate, Kapakaragynan, hydroxypropyl methyl cellulose and guar and increase their concentration acquired (Bouaziz et al . 2010, Guarda et al . 2004).

Table 2: Increase in moisture content compared to control samples

Treatment	Humidity
instance	18.58 ± 3.86
0.1	17.64 ± 4.59
0.15	18.72 ± 3.41
0.2	18.52 ± 3.36

Volume

Gum *Sisymbrium irio* at 1/0, 15/0 2/0% on bread, reduced size compared with the control bread. *Sisymbrium irio* gum may reduce the production of cavities in bread. This reduction could be due to reduced capacity as a result of reducing the amount of gas in the dough gluten.

The results obtained in the investigation (-Bazayz and colleagues in 2010),(Garmyla and colleagues in 2011), as well as liquids .

Table 3: Gum *Sisymbrium irio* at 1/0, 15/0 2/0% on bread, reduced size compared with the control bread

Treatment	Size (cm)
instance	0.00048
0.1	0.00046
0.15	0.00043
0.2	0.00046

Firmness

Hardness, resistance to deformation crumb texture is a characteristic that in most cases is used to assess staling (212) . On the seventh day the most difficult to control bread and the least amount of hard bread with 2.0 percent in the first batch was awarded *Sisymbrium irio* gum. Retrogradation is a function of the difficulty and thus increases with increasing difficulty retrograde.

Table 4: Compare the average impact factor gum Sisymbrium irio difficult and time consuming bread

Seventh	Fifth	Third	First	Repeat Treatment
Aa 1206/6667±78	Bb 248/7500±30	Bb 227/0000±17	Ab 190/3333±70	Witness
Bb 737/3333±206	ABb 331/1667±38	ABc 243/8333±22	Ac 199/0000 ±54	0/1
ABa 984/8333±135	ABb 332/0000±16	Bbc 222/3333±26	Ac 170/8333±69	0/15
Ba 859/3333±118	Ab 490/8333±208	Abc 282/0000±19	Ac 168/0000±61	0/2

Continuity

Back to the flexibility of the tissue and its continuity depends on the initial state. Gum Sisymbrium irio may cause damage to the gluten network structure and causes reversal to the original state. Therefore, the addition of gum Sisymbrium irio reduced coherence factor in bread samples containing gum Sisymbrium irio, against controls. Therefore, by increasing the gum and over time, decreases the staling.

Table 5: Compare the average impact factor gum Sisymbrium irio and time-consuming integration of cake

Seventh	Fifth	Third	First	Repeat Treatment
Aa 0/5433	Aa 0/7100	Aa 0/7367	Aa 0/7033	Witness
Ac 0/4567	Aab 0/7500	Aa 0/8133	Ab 0/7000	0/1
Ab 0/4900	Aa 0/7133	Aa 0/7767	Aa 0/6667	0/15
Ac 0/4833	Ab 0/6600	Aa 0/8033	Aab 0/7267	0/2

A, B and C show a significant difference between the rates on different days and a, b and c indicate the presence of significant differences in different treatments (0/05> p).

The resinous gum

Appendix 3 can be downloaded by examining the sample containing the resinous gum Sisymbrium irio at intervals less than the control sample immediately after cooking. Resinous and other parameters of texture analysis. This parameter assists to digest food and prepare it for swallowing.

Table 6: Compare the average impact factor of gum Sisymbrium irio and time Smghyt bread

Seventh	Fifth	Third	First	Repeat Treatment
Aa 545/3000	Ab 171/3333	Aba 167/3000	Ab 135/9500	Witness
Ba 249/7667	Ab 249/8667	ABbc 198/5333	Ac 137/3000	0/1
Aba 487/0667	Ab 236/3333	Cb 113/8667	Ab 114/4333	0/15
ABa 484/5333	Aab 330/8667	Abc 227/9667	Ac 122/4000	0/2

A, B and C show a significant difference between the rates on different days and a, b and c indicate the presence of significant differences in different treatments (05/0> p).

Image Processing

Compared with the control of bread crumb with gum and increased levels of color which was darker. Since the Maillard reaction is not involved in making the bread crumb color, dark bread crumb is likely caused by gum *Sisymbrium irio*, according to the results obtained by Pooresmaeel due to compression of the grain tissue due to decreased volume, and gum gel formation *Sisymbrium irio* is (Bouaziz et al , 2010).

Table 7: Compare the average impact factor of gum *Sisymbrium irio* and time-consuming brown bread

Seventh	Fifth	Third	First	Day Treatment
a 71/5882±9	a 67/6247±0/992	b 33/9999±0/411	a 83/1372±0/556	Witness
b 74/2353±1	a 76/7451±0/323	d 34/0000±0/327	c 64/1176±0/905	0/1
a 77/3333±2	b 70/3137±0/849	c 40/6656±0/650	b 70/3137±0/849	0/15
a 71/4705±7	a 71/6862±1	b 42/8235±1/979	a 71/6862±1/6861	0/2

a, b and c indicate the presence of significant differences in different treatments (05/0> p).

Results Table (8) , shows that in the control sample had reduced color change over time, while gum samples containing 2.0 *Sisymbrium irio* 15/0 and color changes were observed with the passage of time.

Table 8: Compare the average impact factor of gum *Sisymbrium irio* and time-consuming color variations in bread

Seventh	Fifth	Third	First	Day Treatment
b 2/3068±0/341	b 3/1477±0/357	a 4/7878±0/943	c 0	Witness
a 3/6752±0/321	a 2/9324±0/828	a 3/3964±0/793	a 3/4609±0/749	0/1
ab 5/4265±0/530	a 6/6916±0/754	ab 5/2605±0/974	b 3/8976±0/544	0/15
a 6/8679±1/740	ab 5/8686±1/206	ab 6/2373±1/304	b 4/8385±0/529	0/2

a, b and c indicate the presence of significant differences in different treatments (05/0> p).

Evaluation of Porosity

Results Tables (7) to (8) obtained from analysis of texture images show that by increasing the pore size it reduced *Sisymbrium irio* gum that can be difficult due to reduced volume and increased bread. The mean pore diameter of the holes indicate the area is reduced, decreasing in height and diameter of these changes. These results are consistent with the results of research of S.Han and colleagues (Ozkoc et al . 2009). In addition, during the leavening, the bubbles that are produced during the mixing within the dough expand their gas production by yeast. Thus, the stability of bubbles is most important in that the main cause of instability is connected to individual gas cells. Thick layer of bubbles on the inter connectedness of the dough is reduced (Volpini-Rapina et al . 2012).

Sensory evaluation

Bread properties, such as colour, aroma, taste, are enhanced by increasing the gum *Sisymbrium irio* points respectively. Related to the appearance of bread it is similar to the results obtained in their research confirms that Shalin and colleagues (Mettler et al . 1993, Sidhu et al . 1988). With the increase in chewing ability bread with *Sisymbrium irio*, shows improvement and that corresponds with the results of Guarda and colleagues (Guarda et al . 2004). According to the results of tests to assess the properties of bread, it was found that bread with 1/0 *Drdsdmgh* *Sisymbrium irio* gives the best sensory quality.

Conclusion

Gum *Sisymbrium irio* in increased levels in bread increased hardness, cohesiveness, its resinous, elasticity, and chewiness. Along with cutting ability, brightness, and reduced porosity. Sensory evaluation factors decrease with increasing gum. Reduced volume and crumb and crust color darkening, are the unfavorable characteristics of the gum. It should be noted that treatment with 1.0 per cent Gum *Sisymbrium irio* enhances the sensory properties of bread better than the control sample.

Acknowledgment

With special thanks to the Research and Technology deputy of the Islamic Azad University, shahrood branch.

References

- 1- Appelqvist IAM, Debet MRM. Starch-biopolymer interactions: a review. *Food Rev Int* 1997; 13: 163-24.
- 2- Armero E, Collar C. Texture properties of formulated wheat doughs. *Z Lebensm-Unters Forsch* 1997; 204:136-45.
- 3- Bell DA. Methylcellulose as a structure enhancer in bread baking. *Cereal Foods World* 1990; 35: 1001-1006.
- 4- Bouaziz, M. A., Amara, W. B., Attia, H., Blecker, C., & Besbes, S. (2010). Effect of the addition of de-fatted date seeds on wheat dough performance and bread quality, *Journal of Texture Studies*, 41, 511-531.
- 5- Brady PL and Mayer SM, 1985. Correlation of sensory and instrumental measures of bread texture. *Cereal chemistry* 62(1): 70.
- 6- Collar, C.E. 1996. Retrogradation of the starch fraction in wheat bread. *Food Science and Technol. Int.* 2: 323-333.
- 7- Guarda A, Rosell CM, Benedito C, Galotto MJ (2004) *Food Hydrocolloid*. 18: 241-247.
- 8- Kim, S.K. and D'Appolonia, B.L. (1977a) Bread staling studies. I. Effect of protein content on staling rate and bread crumb content on staling rate and bread crumb pasting properties. *Cereal Chemistry*, 54, 207-15.
- 9- Mettler, E. and Seibel, W. 1993. Effect of emulsifiers and hydrocolloid on whole wheat bread quality. *Cereal chemistry*. 70: 373-377.
- 10- MacRitchie F, Gras PW. 1973. The role of flour lipids in baking. *Cereal Chem* 50: 292.
- 11- Ozkoc, S. O., Sumnu, G., and Sahin, s. 2009. The effects of gums on macro and micro-structure of breads baked in different ovens. *Food hydrocolloids*, 23: 2182-2189.
- 12- Poursmaeil, N. 2010. Formulation and production of prebiotic gluten free bread using transglutaminase enzyme and hydrocolloids: guar and xanthan. M.Sc Thesis, Department of Food Science and Technology, School of Agriculture, Tarbiat Modarres University, Tehran, Iran
- 13- Rojas J.A., Rosell C.M., Benedito de Barber C. 1999. Pasting properties of different wheat flour-hydrocolloids system. *Rojas* 1999. *Food Hydrocolloids* 13, 27-33.
- 14- Sarkar N, Walker LC. Hydration-dehydration properties of methylcellulose and hydroxypropylmethylcellulose. *Carbohydr Polym* 1995; 27: 177-85.
- 15- Selomulyo VO, Zhou W. Frozen bread dough: effect of freezing storage and dough improvers. *J Cer Sci* 2007; 45(1): 1-17.
- 16- Sidhu, S. J. and Seibel, W. 1988. Measurement of chapati texture using Zwick universal testing machine. *Lebensm Wiss. U. Technol.* 21:147-150.
- 17- Volpini-Rapina LF, Sokei FR, Conti-silva AC. 2012. Sensory profile and preference mapping of orange cake with addition of prebiotics Inulin and oligofructose. *LWT Food Science and Technology* 1-6.
- 18- Yarmand, M. S., & Seyedein Ardebili, M. (2005). Effect of Gluten and Malt Flour on Staling and Quality of Barbari Flat Bread. *Iranian, J. Agric. Sci*, 36, 591-602.

Future Accessibility and Assistive Technology Summit Both in Dubai and Doha, this October

After last year's success of Future Accessibility and Assistive Technology Dubai Summit, Advanced Conferences & Meetings is proud to announce the launch of the second edition on 8-9 October 2017 in Dubai, and its first edition in Qatar "Future Accessibility & Assistive Technology Qatar" on 11-12 October 2017 in Doha.

Dubai – A disabled-friendly city by 2020

His Highness Sheikh Hamdan bin Mohammed bin Rashid Al Maktoum, Crown Prince of Dubai, Chairman of the Executive Council, launched the "My Community - A City for Everyone" initiative in November 2013, which aims to fully transform Dubai into a disabled-friendly city by 2020.

Future Accessibility & Assistive Technology Dubai will provide an interactive platform for best practice benchmarking, case study insight sessions, new technology and solution showcase and discussion of challenges and opportunities in the assistive technology sector.

Qatar projects to follow a world class standard for accessibility

In the lead-up and preparation to the FIFA World Cup 2022, the Qatari Government has launched initiatives to transform Qatar into a leading disabled-friendly city by 2020. Working groups have been formed within the Qatari government to develop projects of a world class standard for accessibility in a modern urban environment. This is a key milestone on the roadmap to achieving the Qatar National Vision 2030.

Future Accessibility & Assistive Technology Qatar will support the transition towards a more accessible urban environment by focusing on the principles of universal design that integrate adaptive and assistive technologies to make services, buildings, transportation and activities in Qatar more easily available to all, especially to those with disabilities.

For further information about these two conferences, please visit:
www.futureaccessibility.com for Dubai event or www.futureaccessibilityqatar.com for Qatar event.

