**Brief Communication**

**Screening for hOGG1 S326C variant in normal Saudi population**

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The hOGG1 (MIM 601982) gene is the human homologue of *Escherichia coli* (E.coli), DNA repair protein MutM, which excises 8-oxo-7,8-dihydro 2’deoxyguanosine (8-oxoG) from oxidatively damaged DNA. It is a DNA glycosylase-apurinic (AP) lyase and a member of helix-hairpin-helix (HhH-GDP)-superfamily that nicks the DNA and releases 8-oxoG. It removes 8-oxoG through its glycosylase activity and cleaves the DNA sugar backbone through its lyase activity. The hOGG1 gene is located on 3p26.2 and comprises 7 coding exons and an 8th alternatively spliced exon. The hOGG1 gene has been studied in a number of cancer and normal subjects; several genetic variants have been identified in different populations. The most common polymorphism of hOGG1 is S326C (C>G substitution at position 977 in exon 7). This polymorphism has a different allele frequency among different ethnic groups and may play a role in various types of cancer.

An association between the S326C polymorphism in hOGG1 and increased risk of lung cancer has been reported. Homozygotes for the 326C allele exhibited an increased risk of developing squamous cell carcinoma and non-adenocarcinoma of the lungs compared to heterozygotes for S326C and homozygotes for 326S combined. Furthermore, population-based studies on the association of S326C with lung cancer revealed that the 326C allele confers a 2-fold increased risk of lung cancer. Candidate genetic markers that are indicators for cancer susceptibility may vary in frequency among different ethnic groups. That is why it is important to study the prevalence of these markers in different populations to determine the significance of these markers in increasing cancer susceptibility in different ethnic groups. Polymorphisms of the hOGG1 gene in Saudi individuals have not been studied so far. Assay for these DNA changes in the normal population is an important step towards the documentation of the prevalence of different DNA changes, which can be used as a reference for further studies. The aim of this study was to determine the frequency of S326C in a representative sample of the normal Saudi population. One hundred and fifty blood samples from Saudi individuals were randomly collected from Prince Salman Hospital, Riyadh, Saudi Arabia (consent forms were obtained). The DNA was extracted from whole blood using the QIAamp Blood Maxi Kit (Qiagen) according to the manufacturer instructions. Exon 7 of hOGG1 gene was amplified with the following primers; forward 5’ ACTGTCACTAGTCTCACCAAG 3’ and the reverse 5’ TGAATTCGAAAGGTGCTTGGAAT 3’ to yield a 207 bp product. Polymerase chain reaction (PCR), was performed in a 25 µl reaction using ready-to-go PCR beads (puReTaq, Amersham Biosciences) and 50 ng genomic DNA. Cycling parameters were: 94°C for 3 minutes, 40 cycles of (94°C for 30 seconds, 56°C for 30 seconds, and 72°C for 30 seconds) followed by a final elongation step at 72°C for 1 minute. The PCR products were assayed for S326C polymorphism using *I*ta I restriction enzyme; 10 µl of PCR product was mixed with *I*ta I (10 U) and incubated at 37°C for 3 hours. The digestion products were analyzed by electrophoresis using pre-cast polyacrylamide gels. Bands were visualized by silver staining. The enzyme cuts the mutant allele (G allele) to yield a 100 bp and 107 bp products, while the wild type allele (C allele) remains uncut.

In this study, the frequency of the wild type mutant allele was approximately 0.74:0.26. The results were almost identical to the reported frequencies in the single nucleotide polymorphism (SNP) database of a multiracial group of 657 individuals (frequencies of 0.724:0.276; National Center for Biotechnology Information (NCBI), rs1052133) p-value of 0.5 (χ² value of 0.454 and 95% CI: 0.671-1.209). Moreover, the allele frequencies of the different genotypes in this study (Table 1) were almost identical with those reported in the NCBI database (reported values were 54.3%, 36.3% and 9.6%). In comparison with 5 different ethnic groups, the Saudi group (present study) showed similarities with Caucasians (105 individuals, p-value of 0.45; χ² value of 0.56 and a 95% CI: 0.79 – 1.82) and Hispanic population (23 individuals, p-value of 0.464 using Fisher’s exact test, CI: 0.65-3.08, NCBI rs1052133), but not with the Japanese population (197 individuals, p-value of 0.001; χ² value of 16.1 and a 95% CI: 0.359-0.696) and the Chinese population.

**Table 1** - Genotype for the S326C polymorphism in the Saudi population.

<table>
<thead>
<tr>
<th>Number of chromosomes screened</th>
<th>Genotype Frequency (%)</th>
</tr>
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<tbody>
<tr>
<td>Genotype</td>
<td>Frequency (%)</td>
</tr>
<tr>
<td>S326S</td>
<td>(54.79)</td>
</tr>
<tr>
<td>S326C</td>
<td>(39.73)</td>
</tr>
<tr>
<td>C326C</td>
<td>(5.48)</td>
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</tbody>
</table>
population (98 individuals, p-value of 0.001; χ² value of 58.6 and a 95% CI: 0.678-1.2). The Japanese and Chinese populations had a higher prevalence of the 326C mutant allele than any other population. The Saudi population also showed a marked difference with African American ethnic group (24 individuals, p-value of 0.0262 using Fisher’s exact test, CI 1.135-7.85, NCBI, rs1052133). The prevalence of the 326C allele in the African American sample was very low and the 326C/326C allele frequency was 0%, a variation of what was reported in other populations, but the small number of samples assayed might contribute to the lack of identifying the mutant homozygous allele.

The Kingdom of Saudi Arabia is a vast and an ethnically diverse country. Although, there are pockets of ethnically homogenous populations where there is very little population drift, inter-population differences have been reported for several other genetic loci including sickle cell gene and β-thalassemias. This study showed a significant difference in the genotype allele frequency of hOGG1 S326C in Saudis compared to Chinese and Japanese populations. Further studies are required to genotype the hOGG1 S326C in different regions of Saudi Arabia to document any regional variations and the association of this polymorphism and increased risk of different types of cancer in Saudi Arabia remain to be investigated.

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References


Is Saudi Arabia a fertile land for exchanging infectious diseases?

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Over 2 million people from around the world visit Saudi Arabia every year to perform the Muslim Pilgrimage, Hajj. All of these people congregate at the 2 Holy Mosques in the cities of Mecca and Medina, remaining in crowded environments for up to 3 weeks. A further 2 million people visit the Kingdom to perform Omra in the 2 Holy Mosques. In addition, the country is the home of more than 6 million working expatriates. Most of these visitors, pilgrims and expatriate laborers come from impoverished third world countries where tuberculosis (TB) is endemic. This huge number of expatriates and pilgrims associated with Hajj means that there is a lot of contact between people; more than enough to transfer, spread and exchange communicable diseases. In the past, several outbreaks of meningitis and cholera have occurred, demonstrating transmission of infectious diseases via human-to-human contact. During these visits, a number of people suffer from minor upper respiratory tract infections but there is little consideration for the involvement of serious contagious diseases. One isolated report highlighted the fact that Mycobacterium Tuberculosis, a re-emerging communicable disease, was responsible for cases of pneumonia during Hajj. This report was strengthened by Wilder-Smith et al, when they measured the immune response to TB antigen prior to departure and 3 months after return from Hajj pilgrimage. At the end of Hajj, Pilgrims return to their home countries taking with them any contagious disease they may have acquired. These observations suggest that Saudi Arabia is a fertile environment for the spread and exchange of several indigenous and imported diseases. Previous observations have been reinforced by recent results during an ongoing nationwide epidemiological study. For the last 2 years, we have been able to focus our research efforts on finger-printing M. Tuberculosis in Saudi Arabia. More than 1,400 isolates have been collected and typing is in the final stage. Preliminary data shows many imported clades in Saudi Arabia (previously identified in other parts of the world) such as Beijing, Manila, Latin-America-Mediterranean, Delhi and many others. The presence of several of these families in one country is a strong evidence that the crowding of Hajj and Omra is facilitating the exchange of communicable diseases. There is a paucity of information regarding other diseases but it is unlikely that TB is unique. Further data is required in order to study other communicable
diseases. It is our belief that a committee should be established to monitor this issue that should include any countries from which Pilgrims and immigrants originate. The task of such committee should monitor, raise awareness and potentially initiate screening to minimize the transmission of communicable diseases.

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References


Spontaneous recovery of propylthiouracil-induced fulminant hepatic failure in an 8-year old child

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Hepatotoxicity was first reported as a side effect of propylthiouracil for the treatment of hyperthyroidism in 1947.1 Subsequently, several case studies have been reported.2 Symptomatic propylthiouracil-induced hepatic injury is rare in thyrotoxic adults and less than 10 cases have been published in childhood.3 The clinical course is usually benign once the drug is withdrawn, however, fatal cases have been encountered.4,5 We describe an 8-year-old girl with hyperthyroidism treated with PTU, developed fulminant hepatic failure and ended with spontaneous recovery. An 8-year-old girl presented with 3-week history of heat intolerance, tremor, restless sleep and weight loss. She was noted having diminished school performance due to poor concentration and progressive prominence of her eyes. On examination, her vital signs showed a heart rate of 120 beats/min and blood pressure of 140/89. She had tremor, exophthalmos, and palpable thyroid. The rest of the examination was unremarkable. Laboratory evaluation at presentation showed white blood cell 11.1, neutrophils 40%, lymphocyte 43%, alanine aminotransferase (ALT) 25 U/L (10-35), aspartate aminotransferase (AST) 32 U/L (10-45), alkaline phosphatase (ALK) 203 U/L [normal range (NR) 100-300], gamma glutamyltransferase (GGT) 10 IU/L (NR 7-23), total bilirubin 13 umol/L (NR 0-21), direct bilirubin 3 umol/L (NR 0-5), ammonia 23 umol/L (NR 0-55), prothrombin time (PT) 6 seconds (NR 11.9-14.3), prolonged thrombin time (PTT) 35 seconds (NR 34.7-42.2), free thyroxine (FT4) 91 pmol/L (NR 12-22), total triiodothyronine (TT3) 4.1 nmol/L (NR 1.3-3.1), thyroid stimulating hormone (TSH) 0.02 mU/L (NR 0.27-4.2). Anti-thyroid peroxidase antibody was 189 (normal <12), thyroid stimulating immunoglobulin (TSI) was 150% (normal <120%). Thyroid scan showed diffuse homogenous uptake. She was diagnosed with Grave’s disease and started on PTU 50 mg 3 times per day and propranolol 10 mg 3 times per day.

One month later, FT4 was 30 pmol/L, TT3 was 3.1 nmol/L, and TSH was 0.07 mU/L. 2 months later on the above-mentioned treatment, she presented with progressive yellowish discoloration of sclera, lethargy and fluctuation of her consciousness. Laboratory evaluations showed FT4 24 pmol/L, TT3 2.8 nmol/L, TSH 0.07 mU/L, WBC 8.4, neutrophils 26%, lymphocyte 40%, ALT 161 U/L, AST 144 U/L, ALK 233 U/L, GGT 143 IU/L, total bilirubin 645 umol/L, direct bilirubin 512 umol/L, ammonia 290 umol/L, PT 20.2 seconds and PTT 43.4 seconds. A PTU-induced hepatotoxicity was suspected and PTU was stopped. Potassium iodide (SSKI) 300 mg 3 times a day was started, in addition to hydrocortisone 10 mg 3 times a day. Ultrasound liver showed hepatomegaly with increased echogenicity and normal hepatic blood vessels flow. Liver biopsy showed cholestatic hepatitis with acinar necrosis. Other causes of cholestatic jaundice were ruled out. Serological studies for hepatitis A, B, C, E viruses, cytomegalovirus and Epstein-Barr virus were negative. Metabolic work-up including serum ceruloplasmin level, alpha-1-antitrypsin level, 24-hour urinary copper level and tandem mass spectrometry was unremarkable. Immunological studies indicating autoimmune hepatitis including antinuclear antibody, anti-smooth muscle antibody
and anti-mitochondrial antibody were negative. There was no clinical or biochemical evidence of interstitial nephritis, vasculitis, pulmonary interstitial fibrosis or skin involvement. Two weeks after starting SSKI, FT4 was 14 pmol/L, TT3 was 2.1 nmol/L, and TSH was 0.07 mU/L. Liver enzymes improved gradually to near normal levels over a 4-week period. ALT was 71 U/L, AST was 66 U/L, ALK was 102 U/L, GGT was 36 IU/L, total bilirubin was 43 umol/L, ammonia level was 60 umol/L, PT was 14 seconds and PTT was 37 seconds. The patient continued to be euthyroid and total thyroidectomy was performed followed by thyroxine replacement therapy. A PTU-associated hepatotoxicity is a rare and life-threatening complication of antithyroid drug treatment of hyperthyroidism. The estimated incidence of antithyroid drug-associated hepatotoxicity is less than 0.5%, although the true incidence is unknown. A PTU hepatotoxicity may occur at any age, but it predominates in females. Its occurrence in childhood is extremely rare especially at young ages. We report here an 8-year-old girl with acute fulminant hepatic impairment who spontaneously recovered with supportive management. A PTU-induced hepatotoxicity usually develops within the first few months of PTU administration. The mechanism of antithyroid drug hepatotoxicity is unknown, although positive lymphocyte sensitization studies in some patients who developed PTU hepatotoxicity suggest an immune reaction to PTU. The presentation of PTU hepatotoxicity is clinically nonspecific. However, a search for other potential causes of hepatic dysfunction remains necessary. The clinical presentation may range from subclinical elevations of liver enzymes to severe cholestatic jaundice and encephalopathy. Histologically, nonspecific hepatocellular necrosis is typically found on liver biopsy. Based on the severity of the disease process, the pathological findings may range from early signs of hepatocellular inflammation to submassive hepatic necrosis. In our patient, liver biopsy showed severe hepatocellular necrosis with cholestasis. For unknown reason, PTU usually causes cytotoxic hepatitis while methimazole often causes cholestatic hepatitis.

Kim et al reviewed the medical records of 497 hyperthyroid adult patients treated with PTU. Six patients developed overt hepatitis and 5 patients had cholestatic jaundice. There were no statistical differences in age, gender, PTU dose, or T4 and T3 levels at initial diagnosis between patients with and without hepatic injury. Liver enzymes normalized in all patients between 16 and 145 days after the PTU withdrawal. Our patient had a relatively short course with a smooth recovery 4 weeks after PTU discontinuation. Williams et al reported 7 deaths secondary to PTU-induced hepatotoxicity among 30 cases treated with PTU. Survivors were treated with radioactive iodine and one pediatric case had a liver transplant. They concluded that prompt treatment of the underlying thyroid disease with radioactive iodine may diminish the chance of clinical deterioration from persistent hyperthyroidism and early recognition of the need for liver transplant may improve survival. In our patient, surgical thyroidectomy was preferred as our concern was regarding the oncogenic long-term effect of radioactive iodine and its possible adverse effect on the eye. On the other hand, the patient was on SSKI, which may interfere with radioactive iodine uptake. Upon recognition of hepatotoxicity, PTU should be discontinued. With supportive therapy, most patients should recover. However, death due to complications of liver failure occurred in 25% of the population reported herein. Thus, early recognition of fulminant hepatic failure and intervention are extremely important. Several early prognostic factors are known to be associated with survival rates of less than 20% in fulminant hepatic failure. These include patient age (<11 and >40 years old), duration of jaundice (>7 days) before the onset of encephalopathy, serum bilirubin concentration (>300 µmol/L), and prothrombin time (>50 s). Our patient had at least 3 of these prognostic factors; however she recovered smoothly after PTU discontinuation. The options for treatment of hyperthyroidism in such patients are limited. The PTU is contraindicated due to the unknown mechanism of hepatotoxicity and the reported recurrence of hepatic injury with PTU rechallenge. The majority of patients received definitive treatment with radioactive iodine, and this form of treatment was significantly associated with survival. The ideal treatment may be immediate radioactive iodine therapy when PTU hepatotoxicity is suspected. It was suggested that radiiodine treatment should be completed before the administration of iodine contrast for abdominal computed tomogram scans to evaluate the cause of hepatic dysfunction or iodide therapy for the thyrotoxic state. Propranolol may be used to control the symptoms of hyperthyroidism until radioactive iodine has its full effect. Alternatively, methimazole has been used successfully after hepatic enzyme levels normalize. Amiodarone was used in one patient followed by radioactive iodide. Additional treatment modalities include plasmapheresis, dialysis and liver transplant. Corticosteroids have been used in the management of PTU-hepatotoxicity, although its benefit is doubtful. Hydrocortisone was used in our patient in which was tapered gradually post-operatively. The use of potassium iodide alone after recognition of hepatotoxicity was tried long time ago. The maximal suppression of thyroid hormone levels by potassium iodide is usually produced within 7–14 days and last from 1 to more than 50 days. As iodide can also provide substrate for thyroid hormone synthesis, it is usually used in combination with antithyroid drugs. In our patient, potassium iodide was successfully used alone and produced adequate suppression of thyroid hormones.
Propylthiouracil-induced hepatic failure

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Rimonabant as potential treatment for the neglected epidemic of diabetes in the Middle East and Arabian Peninsula. *Implication for prevention*

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The clustering of insulin resistance, dysglycemia, dyslipidemia, hypertension and central obesity represent the major features of metabolic syndrome. These clusters of factors may share common etiology and each of which is a risk factor for cardiovascular disease. The metabolic syndrome appears to affect between 10 and 25% of adult populations worldwide. Several studies have described the association between metabolic syndrome, diabetes and cardiovascular disease. The prevalence of diabetes for all age groups worldwide was estimated to be 2.8% in 2000 and 4.4% in 2030. The total number of people with diabetes is projected to rise from 171 million in 2000 to 366 million in 2030. The number of people with diabetes is increasing in the Middle East and Arabian Peninsula due to population growth, aging, urbanization, and increasing prevalence of obesity and physical inactivity. Quantifying the prevalence of diabetes and the number of people affected by diabetes, now and in the future, is important to allow rational planning and allocation of resources. In the Arab world, which comprises 22 countries and has a total population of almost more than 300 million, high prevalence of diabetes has been reported from many countries. The estimated prevalence of diabetes has increased in the Arab countries from 2-3% in 1980 to a current prevalence of approximately 20%. In Saudi subjects, the age group of 30-70 years followed for 5 years period between 1995 and 2000. A total of 17,232 Saudi subjects were selected in the study and 16,917 participated (98.2% response rate). Four thousand and four subjects out of 16,917 were diagnosed to have diabetes. This study concluded that the overall prevalence of diabetes in the Kingdom of Saudi Arabia is 23.7%. The prevalence in males was 26.2% while 21.5% in females. Diabetes was more prevalent among Saudis living in urban areas (25.5%) compared to rural Saudis (19.5%). The important conclusion from this study is that 27.9% were unaware of having diabetes. In the light of the observed increase in prevalence of obesity in many countries of the Arab world and Middle East, the number of cases of diabetes currently or in following decades may be considerably higher than expected. Therefore, management of obesity is crucial in order to reduce the epidemic of diabetes. Orlistat, anti-obesity medication was shown to reduce diabetes by 37%. Recent exciting new data suggests that inhibition of endocannabinoid system might be beneficial in the treatment of the metabolic syndrome. The discovery of endocannabinoid system dates back almost 4000 years, when the therapeutic and psychotropic actions of the plant Cannabis sativa were first documented. The endocannabinoid system contributes to the physiological regulation of energy balance, food intake, lipid and glucose metabolism through both central and peripheral effects. Many different regulatory actions
have been attributed to endocannabinoids, and their involvement in several pathophysiological conditions is under intense scrutiny. Cannabinoid receptors, named cannabinoid-1 receptor (CB1) and cannabinoid-2 receptor (CB2), participate in the physiological modulation of many central and peripheral functions. The CB2 receptor is mainly expressed in immune cells, whereas CB1 receptor is the most abundant G protein-coupled receptor expressed in the brain. The CB1 receptor is expressed in the hypothalamus and the pituitary gland, and its activation is known to modulate all the endocrine hypothalamic-peripheral endocrine axes. An increasing amount of data highlights the role of the system in the stress response by influencing the hypothalamic-pituitary-adrenal axis and in the control of reproduction by modifying gonadotropin release, fertility, and sexual behavior. The ability of the endocannabinoid system is to control appetite, food intake, and energy balance by modulating rewarding properties of food by acting at specific mesolimbic areas in the brain. In animal models, CB1 blockade by rimonabant produces a lean phenotype, with resistance to diet-induced obesity and associated dyslipidemia. In the hypothalamus, CB1 receptor and endocannabinoids are integrated components of the networks controlling appetite and food intake. The endocannabinoid system was recently shown to control metabolic functions by acting on peripheral tissues, such as adipocytes, hepatocytes, the gastrointestinal tract, and, possibly, skeletal muscle.4,5 The Rimonabant in obesity (RIO)-Europe study4 recruited patients with body mass index (BMI) of 30 kg/m² or greater, or BMI greater than 27 kg/m² with treated or untreated dyslipidemia, hypertension, or both, were randomized to receive double-blind treatment with placebo, 5 mg or 20 mg rimonabant (currently licensed in Europe), once daily in addition to a mild hypocaloric diet (600 kcal/day deficit). The primary efficacy endpoint was weight and change from baseline after 1 year of treatment in the intention-to-treat population. Weight loss at 1 year was significantly greater in patients treated with rimonabant 5 mg (mean -3.4 kg [SD 5.7]; p=0.002 versus placebo) and 20 mg (-6.6 kg [7.2]; p<0.001 versus placebo) compared with placebo (-1.8 kg [6.4]). Significantly, more patients treated with rimonabant 20 mg than placebo achieved weight loss of 5% or greater (p<0.001) and 10% or greater (p<0.001). Rimonabant 20 mg produced significantly greater improvements than placebo in waist circumference, high density lipoprotein (HDL)-cholesterol, triglycerides, and insulin resistance, and prevalence of the metabolic syndrome. The effects of rimonabant 5 mg were of less clinical significance. Rimonabant was generally well tolerated with mild and transient side effects.4

The RIO-lipids study5 randomly assigned 1036 overweight or obese patients (BMI was between 27-40) with untreated dyslipidemia (triglyceride levels >1.69 - 7.90 mmol per liter, or a ratio of cholesterol to HDL-cholesterol of >4.5 among women and >5 among men) to double-blinded therapy with either placebo or rimonabant at a dose of 5 mg or 20 mg daily for 12 months in addition to a hypocaloric diet. Their result showed, as compared with placebo, rimonabant at a dose of 20 mg was associated with a significant (p<0.001) mean weight loss (repeated-measures method, -6.7±0.5 kg, and last-observation-carried-forward analyses, -5.4±0.4 kg), reduction in waist circumference (repeated-measures method, -5.8±0.5 cm, and last-observation-carried-forward analyses, -4.7±0.5 cm), increase in HDL cholesterol (repeated-measures method, +10.0±1.6 %, and last-observation-carried-forward analyses, +8.1±1.5 %), and reduction in triglycerides (repeated-measures method, -13.0±3.5 %, and last-observation-carried-forward analyses, -12.4±3.2 %). Rimonabant at a dose of 20 mg also resulted in an increase in plasma adiponectin levels (repeated-measures method, 57.7%, and last-observation-carried-forward analyses, 46.2%; p<0.001), for a change that was partly independent of weight loss alone.5 The most frequent and important adverse events resulting in discontinuation of the drug were depression, anxiety, and nausea. These side effects may be important as obesity per se is often associated with depression and low self-esteem. Another important issue is that caution is needed with administration of this medication in patients with moderate liver failure. As fatty liver now appeared as common liver abnormality with obesity, further studies are needed to address the safety of administration of rimonabant in such individuals. In addition, rimonabant reduced metabolic syndrome and half of the effect on HDL and triglyceride was independent of weight loss. This was attributed to an associated increase in adiponectin. It will be of interest to determine whether long term administration of rimonabant will be associated with a reduction in the prevalence of diabetes and cardiovascular disease, especially in the Middle East and Arabian Peninsula. Research testing of this hypothesis may have an important impact in treating metabolic syndrome and associated risk of development of diabetes. This may provide potential for developing part of health strategies towards the prevention of the epidemic of diabetes.

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Five-year surveillance of chickenpox in Qassim, Central Saudi Arabia


Chickenpox or Varicella results from primary infection with varicella zoster virus. The resulting illness is usually mild, but serious complications and deaths can occur. Amongst children, generally it is a mild illness but rare complications such as pneumonia, encephalitis and acute cerebellar ataxia may occur. Chickenpox is an important public health problem because it is very common, highly contagious and carries a high secondary attack rate. It leads to untoward health and economic consequences. A live-attenuated varicella vaccine is available, has proven to be safe and effective, and introduced in some countries around the world. In the Kingdom of Saudi Arabia, chickenpox is a notifiable disease. According to the Ministry of Health Communicable Diseases Report 2003, the reported cases demonstrate a rise during the years 2000 to 2003.\(^1\) In Saudi Arabia, the vaccine for varicella is not included in the routine childhood immunization program. At this point in time, when there is a debate regarding introduction of universal varicella vaccination in Saudi Arabia,\(^2\) insight into the epidemiology of chickenpox will also be helpful to formulate an appropriate strategy for implementation and evaluation of the vaccination program. This study describes the magnitude of the problem as well as epidemiological factors of chickenpox in Qassim region for 5 years period; from 1999 to 2003.

It is a descriptive analysis of surveillance data of chickenpox, collected by the Preventive Medicine Department, Primary Health Care Administration, Qassim region. Qassim, located in the northern part of the center of Kingdom of Saudi Arabia, covers an area of 78,500 Km\(^2\). According to the Third National Census of Population and Housing, its population was 1.016 million during the year 2004.\(^3\) Non-Saudis comprised 19.6% of the population, majority of them, being adults constituting the expatriate work force. The list of Notifiable Diseases in Qassim region follows the list of Ministry of Health and includes chickenpox as a notifiable condition. The surveillance data for notifiable diseases has been computerized in Qassim since January 1999. Reporting of notifiable diseases to the Preventive Medicine Department is “passive”, that is the department relies on health care providers in health care facilities to report disease occurrence. All health care facilities; primary, secondary and tertiary, whether public or private, are obliged to submit weekly report of notifiable disease cases to the primary health care administration. The data included age, gender and nationality of the cases. Other variables were reporting week, name of reporting health care facility and district. Analyses were conducted using the Statistical Package for Social Sciences version 10. The distribution of cases was examined by age, gender and nationality. Between 1999 and 2003, 20,788 cases of chickenpox were reported and provided the basis for the analysis. Overall, the incidence rates increased from 207 per 100,000 population in 1999 to 759 per 100,000 during

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References

Five year surveillance of chickenpox in Qassim, Central Saudi Arabia

The incidence rates in Saudis increased from 245 per 100,000 in 1999 to 918 per 100,000 in the year 2003. In case of non-Saudis the incidence rates for 1999 and 2003 were 51 per 100,000 and 107 per 100,000. A sharp rise in the absolute number of cases can be noticed since the year 2000 (Figure 1). The number of cases increased from 1611 in 2000 to 7532 in the year 2003-more than 4-fold increase.

Table 1 displays the numbers of incident cases of chickenpox by gender and age-group for the period 1999-2003. Chickenpox was reported in 11324 (54.5%) males and 9464 (45.5%) females. The highest proportion (36.8%) of notifications for chickenpox cases occurred in the 5-9 age group. Approximately 78.5% of the reported cases were below age 15. Children <5 years constituted 2955 (14.2%) cases and 52 (0.3%) cases were >65 years. Saudis constituted 20,034 (96.4%) of the notified cases, while 752 (3.6%) were non-Saudis. In 2 reports, nationality was not recorded. The weekly distribution of chickenpox in the region showed a seasonality pattern with higher incidence between 9th and 26th weeks of the year, corresponding to the months of March-June. More than one-third (43.7%) of the cases was reported during these months. There was then a decline from June through September. A rise in number of cases was noticed again starting from the 38th week namely mid-September and was continuous until the end of the year. The highest number [10,004 (48.1%)] of cases were reported from Primary Health Care Centers, followed by 5,752 (27.7%) cases from other government institutions, then from hospitals 3,296 (15.9%) cases were reported and least [466 (2.2%)] by private institutions. The reporting health care facility of 1270 (6.1%) cases was not recorded. Our study shows an increasing incidence of chickenpox in the Qassim region during the study period. This finding is in accordance with the results reported in other published literature.1,2 The lower incidence rates amongst non Saudis can be explained by the fact that chicken pox is mainly a childhood disease and majority of non Saudi population comprises of adult working age group. Although the incidence of disease was reported to be similar in both gender in most of the medical literature,4,5 the number of cases is significantly (p<0.0001) higher in males in our study. Several studies carried out in the prevaccination era in developed countries have reported that varicella was most frequently seen between ages 4 and 10 years. In our study also, the highest proportion (36.8%) of cases are reported in the age group 5-9 years. In France and USA, during prevaccination era, approximately 90% of chickenpox cases occurred in children <15 years of age. In contrast, in our study the percentage of chickenpox cases <15 years was 78%, which is consistent with other reports from Saudi Arabia, demonstrating 16-25% of chickenpox occurring in adults, and 15-20% of adults being seronegative.6 Various studies from developed countries have mentioned that the age distribution of chickenpox appears to be changing, with more cases being reported in children aged 0-4 years.7,8 Some researchers have attributed this change to increased social mixing in pre-schoolers, allowing greater opportunity for virus transmission.8 Others have attributed it to the possibility of an overall decline in transmission or increasing rates of mild or sub clinical infection in under 5-age group.4 However, the proportion of cases in 0-4 age group in our study remains almost stable during the study period. This might be explained by

Table 1 - Distribution of cases of chickenpox by gender and age-group in Qassim, Kingdom of Saudi Arabia (1999-2003).

<table>
<thead>
<tr>
<th>Age-group</th>
<th>Males</th>
<th>Females</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1 year</td>
<td>158 (1.4)</td>
<td>158 (1.7)</td>
<td>316 (1.5)</td>
</tr>
<tr>
<td>1-4 years</td>
<td>1433 (12.7)</td>
<td>1206 (12.7)</td>
<td>2639 (12.7)</td>
</tr>
<tr>
<td>5-9 years</td>
<td>4193 (37.0)</td>
<td>3461 (36.6)</td>
<td>7654 (36.8)</td>
</tr>
<tr>
<td>10-14 years</td>
<td>3069 (27.2)</td>
<td>2644 (27.9)</td>
<td>5713 (27.5)</td>
</tr>
<tr>
<td>15-19 years</td>
<td>1338 (11.8)</td>
<td>976 (10.3)</td>
<td>2314 (11.1)</td>
</tr>
<tr>
<td>20-24 years</td>
<td>423 (3.7)</td>
<td>384 (4.1)</td>
<td>807 (3.9)</td>
</tr>
<tr>
<td>25-44 years</td>
<td>587 (5.2)</td>
<td>541 (5.7)</td>
<td>1128 (5.4)</td>
</tr>
<tr>
<td>45-64 years</td>
<td>94 (0.8)</td>
<td>63 (0.7)</td>
<td>157 (0.8)</td>
</tr>
<tr>
<td>65+ years</td>
<td>25 (0.2)</td>
<td>27 (0.3)</td>
<td>52 (0.3)</td>
</tr>
<tr>
<td>Unknown</td>
<td>4 (0.0)</td>
<td>4 (0.0)</td>
<td>8 (0.0)</td>
</tr>
<tr>
<td>Total</td>
<td>11324 (100)</td>
<td>9464 (100)</td>
<td>20788 (100)</td>
</tr>
</tbody>
</table>
the fact that the majority of children are exposed to the virus in their schools as the culture of day cares and preschool nurseries is not much prevalent in this region. In our study, distinct seasonality pattern was observed as also reported by other researchers. Varicella is reported to be more common in the spring and winter season it was also observed in this study. Biases are inherent in a passive surveillance system that relies on reporting from health care providers. Not all chickenpox cases, from the community submit reports to the health care facilities that lead to underestimation of the problem size. Similarly, chickenpox cases may not be notified to the preventive medicine department. These factors need to be identified and investigated.

Our study concludes that there is a substantial increase in reported cases of chickenpox in Qassim and routine varicella immunization will definitely decrease the incidence and severity of disease. However, decision making should depend on special studies to determine the true incidence and severity of chickenpox, its seroprevalence and cost-effectiveness of immunization.

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References