Influence of sickle hemoglobinopathy on growth and development of young adult males in Southern Iraq

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Patients with sickle cell disease (SC) turned to have weight (wt), linear growth and sexual maturation delay based on data from other countries.[1,2] By 2 years of age, children with sickle cell disease (SCD) have detectable growth retardation, which affects weight more than height and has no clear gender difference.[1] Normal height is achieved by adulthood, but weight remains lower than that of controls. More severe growth delay and retarded sexual maturation is noted in children with sickle cell anemia and sickle cell-β^0-thalassemia while Hb SC disease is associated with a less severe growth delay. Skeletal maturation is also delayed. The aim of the study is to assess the wt, linear growth, BMI and sexual maturations of young adult males patients in Basrah (Southern Iraq). Males patients with SCD attending the out patients clinic of Basrah Military hospital were included in this cross-sectional case control study from January 1999 to December 2001. The diagnosis was based on criteria mention elsewere.[1] The total number of patients were 75, all males aged 18 years. They were 62 sickle cell anemia (SCA) and 13 sickle cell β-thalassemia (Hb S/βthal), of them 12 Hb S/β+ thal and 1 Hb S/β^0 thal. The control was also 75 males, all aged 18-years attained the hospital for premployment routine examination. Anthropometry: height (ht) was taken while standing, wt taken with light clothes. The wt measurement is measured to nearest 100 grams and ht to the nearest 0.25 centimeters. The United States of America national center for health statistics (NCHS) is taken as references for ht and wt of patients in order to study the physical growth of patients.[3] Body mass index calculated according to formula wt (kg)/ht (m^2). Measurement of maturation: each male was assessed in a private room for secondary sex characters by comparing the body to drawing of Tanner stages. Combined genital and pubic hair staging taken as sum of both stages divided by 2. For statistical analysis Chi-square test used as appropriate. Comparison between 2 means is carried out using unpaired student t-test and between more than one mean is carried out using one-way analysis of variance (ANOVA). Level of significance was set to be <0.05 through out analysis. There were no significant differences in the both ht and wt among the 2 different genotypes of SCD. For the wt, 77.3% of SCD were in the wt band below the 5th centil and none of them reached to 50th centil. While for the ht 46.6% of SCD are in the ht band <5th and only 4% of them reached to the ≥50th centile. Comparison between patients wt, ht and BMI made with that of control is in **Table 1**. Very significant differences (p<0.00001) between both wt and ht of patients with that of control in 2 centile bands of <5th and ≥ 50th. Seventy seven point three percent of patients wt were in the <5th band versus 10.6% of control lies in this band, and 46.4% of patients with 8% of control lies in the <5th band of ht. None of patients having wt ≥ 50th but 24% of control are (p<0.00002), and only 4% of them having ht ≥ 50th versus 57.3% of control (p<0.00001). The BMI of control and patients were 21.2 ± 3 and 16.9 ± 2.8 which were highly significant differences (<0.0001). Those with under wt (BMI <20) constitute 78.6% of patients and 38.6% of control (p<0.00001). No difference in combined Tanner stages between the 2 genotypes of SCD. Only 54.6% of patients reached to stage 5. The others lie in stages 2-3. Regarding Tanner staging system, comparison between combined pubic and genital stage between patients and control showed that all the control was in stage 5, but only 54.6% of patients reached to stage 5 (p<0.00001). There were 25.3% of patients in stage 4 (p<0.00001), 12% in stage 3 (p 0.005) and 8% in stage 2 (p<0.03) The relation between centil band and clinical characters is present in **Table 2**. Patients with wt and ht lie <5th band are more likely to have bone deformity, splenomegaly, blood transfusions, painful crisis, and hospitalization. **Table 3** shows the relation between the mean Hb (hemoglobin) level, mean Hb S, Hb F in comparison with centil band of the wt and ht. Patients with lower centil band of wt tend to have lower mean Hb level (p<0.0001) and the same applied for ht (p 0.0003). Those with a lower centil band of wt tend to have higher level of Hb S level (P<0.0001), but this not significant when applied for ht. Those with a lower centil band for wt have higher mean Hb F (p 0.01) but again for ht the differences are not significant. All the patients in this study did not reach to the 50th centil band for wt, and the wt affected more than the ht. This is also seen in previous studies.[1] It's mentioned that in sicklers, normal height is achieved by adulthood, but in this study, 96% of patients failed to reached the normal adults ht (50th band) by the age of 18-years. For sexual maturations, 45.3% of the patients failed to reach the maturation. In general, boys with SCD have delayed sexual maturation that is more severe in those with SCA than in those with Hb SC disease. The retarded sexual maturation in males can be due to primary hypogonadism, hypopituitarism, or hypothalamic insufficiency. At least one study from the Kingdom of Saudi Arabia showed gonadal hypofunction in the sickle cell patients.[2] While other opinion considered the cause of sexual immaturity inpatient with SCD is constitutional rather than a primary endocrinologics, and even there is elevated gonadotropin levels for the stage of sexual development.[1] Patients with growth retardation in this study turn to have more bone deformity, splenomegaly, blood transfusions, painful crisis and hospitalization. Delayed growth and sexual maturation correlates with the degree of hemolysis in patients with

Table 1 - Comparison between patients and control weight and height.

Variables Centil band	Patient-weight (N=75)	Control-weight (N=75)	p-value	Patient-height (N=75)	Control-height (N=75)	p-value
<5th n (5)	58 (77.3)	8 (10.6)	<0.00001	35 (46.6)	6 (8)	<0.00001
5-9th n (%)	6 (8)	19 (25.3)	0.008	3 (4)	1 (1.3)	0.6
10-24 n (%)	8 (10.6)	15 (20)	0.17	15 (20)	12 (16)	0.6
25-49th n (%)	3 (4)	15 (20)	0.005	19 (25.3)	13 (17.3)	0.3
≥50th n (%)	0 (0)	18 (24)	<0.00002	3 (4)	43 (57.3)	<0.00001
Body mass index - mean ± SD (kg/m2)	16.9 ± 2.8	21 ± 3	<0.0001	-	-	-
**Body mass index	59 (78.6)	29 (38.6)	<0.00001	-	-	-

** Underweight

Table 2 - Comparison between clinical parameters and centil bands for weight and height.

	Centil band									
	<5th n (%)		5-9th n (%)		10-24th n (%)		25-49th n (%)		≥50th n (%)	
Clinical character	Wt	Ht	Wt	Ht	Wt	Ht	Wt	Ht	Wt	Ht
Bone deformity (N=24)	21	14	1*P <0.00001	0*P <0.00001	2*P <0.00001	3*P =0.002	0*P <0.00001	7*P <0.00001	0*P =0.07	0*P <0.00001
Splenomegaly (N=37)	29	17	2*P <0.00001	2*P =0.0001	3*P <0.00001	3*P =0.0004	3*P <0.00001	12*P =0.3	0*P <0.00001	3*P =0.0004
Blood transfusions (N=51)	40	27	4*P <0.00001	1*P <0.00001	6*P <0.00001	9*P =0.0003	1*P <0.00001	13*P =0.01	0*P <0.00001	1*P <0.00001
Painful crisis (N=40)	30	19	3*P =0.00003	1*P <0.00001	6*P <0.00001	6*P =0.003	1*P <0.00001	13*P =0.2	0*P <0.00001	1*P <0.00001
Hospitalization (N=47)	34	21	4*P <0.00001	2*P <0.00001	7*P <0.00001	8*P 0.006	2*P <0.00001	14* =0.2	0*P <0.00001	2*P <0.00001

Wt - weight, Ht - height

Table 3 - Relations between means hemoglobin, mean levels of hemoglobin S, and F with centile band. ANOVA - analysis of variance.

	Centil band										
	<5th Mean ± SD		5-9th Mean ± SD		10-24th Mean ± SD		25-49th Mean ± SD		≥ 50th Mean ± SD		p-value
	Wt	Ht	Wt	Ht	Wt	Ht	Wt	Ht	Wt	Ht	
Mean Hb ± SD	4 ± 1.6	8 ± 1.6	8.7 ± 1.4	8.8 ± 0.3	9.9 ± 1.5	8.4 ± 1.4	9.9 ± 2.7	9.5 ± 1.3	0	9.7 ± 2.3	WT<0.0001 HT 0.003
Mean Hb S ± SD	7.2 ± 8.5	78.5 ± 8.6	78 ± 6.5	75.8 ± 4.6	76.7 ± 5.7	75.4 ± 8.4	72 ± 2.5	74.7 ± 6.2	0	74.9 ± 0.2	WT <0.0001 HT 0.4
Mean Hb F ± SD	18.2 ± 9.4	17.8 ± 9.6	18.1 ± 6.5	16 ± 1.6	25.1 ± 7.2	19.6 ± 8.8	16.3 ± 5.8	21.8 ± 6.2	0	14.1 ± 4.8	WT 0.01 HT 0.7

Hb - hemoglobulin, Wt - weight, Ht - height

SCD due to the increased basal metabolic requirements of a patient with hemolysis.[4] The hypermetabolic state will require greater dietary energy compared with Hb AA. In this study patients with growth retardation tends to have lower mean Hb.

It has been possible to restore normal growth by nutritional supplementation. There have been reports of responses to folic acid, zinc supplementation or regular blood transfusion, but these approaches are not recommended as standard care. A high concentration of fetal Hb in boys with SS disease is associated with greater linear growth. It is postulated that in boys, low concentrations of fetal hemoglobin increase hemolysis and hence metabolic requirements for erythropoiesis, putting them at greater risk of poor growth.[5] In this study patient with higher Hb F tend to have more underweight, and no explanation available for this paradoxical finding, whoever most agree that the relation between HbF level and clinical severity of SCD is not simple.[1]

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Effect of itraconazole therapy in allergic bronchopulmonary aspergillosis

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Allergic bronchopulmonary aspergillosis (ABPA) is characterized by type I and type III hypersensitivity reactions to *Aspergillus* antigen. Incidence of ABPA among bronchial asthma has been found to vary from 3.7-11% in western countries. Kumar and Gaur[1] has found prevalence of ABPA in patients of chronic bronchial asthma as 16%. It appears that excessive mucus and inflammation may lead to germination and colonization of *Aspergillus* in the airways. This leads to a constant supply of antigen thereby causing inflammation and attracting eosinophils and lymphocytes. Oral corticosteroids are still the mainstay for treating ABPA. These drugs decrease the airway inflammation; increase the body's efficiency in clearing the organism and decreasing the bronchial environment suitability for *Aspergillus* growth. Despite these benefits, it is well known that corticosteroids have a serious long-term adverse effect. Itraconazole is a highly lipophilic triazole derivative active against *Aspergillus* both in vitro and in vivo. The drug blocks the sterol synthesis pathway in the lungs. Itraconazole also seems to have a more benign adverse effect profile than other oral antifungals such as amphotericin B, hamycin and ketoconazole. Most patients can tolerate the drug with few adverse effects. Itraconazole has not been used much in India. Hence, we present 2 cases where Itraconazole was given and the response was good.

A 21-year-old man (height 164 cm, weight 41 kg) with a bronchial asthma since childhood and increasing in severity over times. At the age of 16 years, he complained of high grade fever with evening rise without any cough or hemoptysis. These symptoms persisted for 2-3 weeks, and the patient was diagnosed as having pulmonary tuberculosis based on chest radiograph abnormalities. No other investigations were carried out. He was put on anti-tuberculosis treatment; a Rifampicin based regimen was started which the patient took with good compliance. After 18 months, the treatment was stopped due to poor response. At the age of 20 years, the patient had complaints of cough with hemoptysis (2-3 episodes per day) and anorexia with significant weight loss. There was no fever. The chest radiographs were within the normal limits and sputum was negative for acid fast bacilli (AFB). Antitubercular drugs was started. Patient took Rifampicin, Streptomycine, Pyrazinamide, Ethambutol for 3 months followed by Rifampicin, Pyrazinamide, Ethambutol for next 3 months. Subsequently, he was taking only Rifampicin which he was still continuing at the time of presentation in September 1997 at our Institute (Vallabhbhai Patel Chest Institute, University of Delhi, Delhi, India). The hemoptysis had subsided by then. On investigation, the laboratory findings showed eosionophilia in peripheral blood. Sputum samples were repeatedly negative for AFB. The chest radiographs showed consolidation in the right upper zone. The previous x-ray was examined showed fleeting shadows. A cavity was seen in the left upper zone. Spirometry showed an forced vital capacity (FVC) of 45%, forced expiratory volume at one second (FEV1) - 45% and the ratio of FEV1/FVC was 92%. The serum precipitins against *Aspergillus fumigatus* and *Aspergillus flavus* were positive. The total immunoglobulin (Ig) E was raised. Specific IgE and specific IgG against *Aspergillus fumigatus* were detected. Sputum culture was negative for any pathogenic fungus. The skin test was positive (immediate and late) for *Aspergillus fumigatus*. The

computerized tomography scan of the lung showed cavity on left and central bronchiectasis. There was presence of fibrotic lesions and pleural thickening on the left side. Based on these findings; a diagnosis of ABPA was made and patient was given an oral prednisolone (40 mg/day) with a gradual tapering of dose for a total period of 3 months. The patient did not improve. Along with prednisolone, Itraconazole (200 mg once daily) was given for period of one year. Serological improvement was also observed as the serum was negative for precipitins against aspergillus although specific IgG was still detectable. The eosinophilia also subsided. The patient improved symptomatically. The patient is still being followed up and has no fresh complaints.

A 39-year-old female (height 147 cm, weight 67 kg) had complaints of breathlessness with wheeze, cough with expectoration and a history of frequent nasal and eye symptoms for the last 15 years. Her son is an asthmatic patient. During investigation, her peripheral blood showed eosinophilia. Spirometry showed a FVC of 54%, FEV_1 of 53% and the ratio of FEV_1/FVC 97% which improved after a bronchodilator; for example FVC of 65% FEV_1 of 57% and the ratio being FEV_1/ FVC 88%. Serum precipitins against *Aspergillus fumigatus* were detected. Specific IgE and IgG against *Aspergillus fumigatus* were detected. Skin tests against *Aspergillus fumigatus* antigen were positive (immediate and late), x-ray was normal. The patient was given oral prednisolone (40 mg/day) which was gradually tapered off during a total period of 4 months. The patient improved. After approximately one year she again had an exacerbation of symptoms, and serologically she was positive for ABPA. She did not want to take Prednisolone as previously since her weight increased due to Prednisolone. She was given itraconazole (200 mg per day) for 8 months. Patient showed improvement symptomatically. The serological parameters have also reduced. There were no fresh complaints. Oral corticosteroids has been widely used for the treatment of ABPA to prevent acute episodes as well as to decrease the likelihood of irreversible lung damage. These agents suppress the allergic and inflammatory responses associated with the bronchial colonization by *Aspergillus*. The effectiveness of a systemic antifungal treatment of ABPA was shown by Shale et al[2] in using ketoconozole. Itraconazole, a new triazole with less toxicity has more activity against *Aspergillus species* than ketoconazole. Some studies of ABPA being treated with itraconazole have been reported. Denning et al[3] reported a study of 6 patients with ABPA treated with Itraconazole 200 mg twice a day for a mean of 3-9 months.[5] Five out of 6 patients were receiving corticosteroids simultaneously. By 2 months the mean oral corticosteroid dose was reduced; lung function improved and there was a significant decrease in total IgE levels. During 6 months of follow-up after treatment; one patient suffered acute ABPA and another had an asymptomatic rise in IgE.

In another case reported by Pacheco et al[4] a corticosteroid dependent patient with ABPA treated with itraconazole had a steroid sparing effect as well as improved lung function and decreased IgG to Aspergillus.

In a case report by Nikado et al[5] a patient was originally diagnosed with ABPA at the age of 19 and treated successfully with 4 weeks of oral prednisolone. For a relapse approximately 4 years later, the patient refused prednisolone due to secondary weight gain. After 2 weeks of itraconazole (100 mg per day) the patient showed symptomatic and serological improvement and after 6 weeks of treatment there was improvement in chest x-ray. In another study by Salez et al,[6] 14 patients of ABPA were treated with itraconzole for one year (200 mg per day). Clinical, serological and functional improvement was observed as well as the need for corticosteroid treatment was reduced or eliminated. Our study in 2 patients also showed clinical serological and functional improvement with itraconazole. There were no side effects observed with the drug.

In conclusion, we suggest that Itraconazole is useful in the prevention of ABPA exacerbations and treatment with Itraconazole may have a corticosteroid sparing effect leading to reduction or elimination of use of corticosteroids in management of ABPA. However, randomized controlled studies are required to determine the role of Itraconazole in a long term management of ABPA.

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Socio-economic discrepancies in growth status of Jordanian children in military-run schools at the turn of the twentieth century

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The State of the World's Children, 1996, reported by the UNICEF[1] showed that the percentage of Jordanian children under-5 (1980-1994) suffering from moderate and severe underweight, wasting and stunting was 9%, 2% and 16%. Growth-restricted children have significantly poorer performance than non-growth-restricted children on a wide range of cognitive test.[2] To assess differences in health and nutrition between groups in a population, growth charts have to be locally established. Until local charts are available, the use of the available Centers for Disease Control/United States of America (CDC/USA)growth charts[3] permits international comparisons of the impact of various environmental factors, such as poverty and infection on the overall growth of children.

We have undertaken a survey to measure multiple health indicators in school children aged 6.5-17.5 years, among which were height and weight in addition to other socio-economic indicators. The purpose of this paper is to investigate the extent of differences in BMI in both urban and Southern Badia Jordanian school children, and compare them with CDC/USA standards. Military-run schools are spread all over Jordan and open for all citizens. Only 16.2% of the students in these schools have a parent who is a member of the Armed Forces, while the rest have civilian parents. The present report deals exclusively with different BMI among male students from 2 socio-economically-distinct regions: the poor Southern region and the better off middle urban region including the capital Amman and Zarka city, Jordan. Socio-demographic data were obtained using a structured questionnaire prepared specifically for the purpose of this study. Questionnaires were distributed to the students who were asked to pass them to their parents to be completed and returned in the next day. Measurement of height and weight in standardized methods and recorded the nearest 0.1cm and 0.1kg. Data were entered into computer using DB3 Plus software and analyzed using the Statistical Package for Social Sciences. **Table 1** presents the socio-economic characteristics of the students in the middle and Southern regions. Consanguinity was more common in the Southern than the middle region (65% versus 50%) P= 0.001. Southern students tend to belong to families with lower educational levels, lower incomes and a larger number of children.

The total number of boys was 5223 distributed in the 2 regions, the middle region 2762 (52.9%) and Southern Badia of Jordan, 2461 (47.1%). A demographic description and the average family income in Jordanian Dinars (JD)/month of the study population is given in **Table 1**. The most economically underprivileged groups in the population under study are those living in the Southern Badia region, were only 1.2% of the population had an income of more than 351 JD/ month, and 69% had an income of less than 150 JD/month. Sixty percent of the students were products of consanguineous marriages. The number of siblings per family among the study population was 7.3; it accounts for 8.5 in the Badia region and 6.1 in the urban area. This study showed the BMI status of Jordanian school children aged 6.5-17.5 years. There are obvious discrepancies demonstrated between the urban and Southern Badias'Jordanian school children in their BMI, which, are likely to be of some relevance to practicing clinicians and to the decision makers. Jordanian school children living in the Southern Badia region have significantly lower BMI <5th percentile (P<0.005), than their counterpart living in the urban region at all age groups understudy. Growth is the result of the interaction of genetic makeup, nutritional factors, hormones, metabolism and cerebro-cortical influences.[4] Consanguineous mating in Jordan was reported by Khoury and Massad[5] to be 50% among Moslems and Christians, but reached 50% and 65% in the urban and Southern Badia in the current study. If any measure is to be taken to improve the growth parameters of children from the Badia region, it should be very early on life, as, benefits to growth occurred when intervention began in pregnancy and continued for at least the first 3 years of life.[6]

It is worrisome that obesity (BMI> 95th centile) among Jordanian school children living in urban region

Table 1 - Socio-economic characteristics of the study population.

Variables	Middle region (N=2762)	Southern region (N=2460)	p-value
Consanguinity between parents	(50)	(65)	
Fathers' education. Primary school or less	(8.1)	(30.4)	0.48
Mother's education. Primary school or less	(13)	(74.2)	0.04
Family income (JD/month.)*			
≤150	(25.2)	(69)	
151-250	(39.3)	(23.2)	
251-350	(21.1)	(6.6)	
≥351	(14.4)	(1.2)	
Mean number of sibling/family	6.13	8.51	0.003

*Jordanian Dinars = 1.4 USA Dollars

is 3.9%, 10.9%, and 5.7% at 6.5, 13.5 and 17.5 years of age in comparison with their age matched children whose BMI 0.7%, 2.2% and 0.8%. This may be related to the lack of activity among Jordanian school boys living in the urban region and the tendency to stay at home where an increased amount of time is being spent viewing television as a pastime and less time spent in sport activities. It has been reported that decreasing television, videotape and video game use may be a promising population-based approach to prevent childhood obesity.[7] It is open to question if large size is advantageous. Although in the recent past, the best nutrition has often been equated with the most food that can be obtained, it is now accepted that too much may be harmful as too little.[8] As these schools are open to all sectors of the population, we have no reason to believe that our children are different from the rest of school children in the country. It is hoped that the present study will encourage the health authorities in Jordan to conduct national growth studies in the country aiming towards constructing national standards for growth of Jordanian children to replace the international reference growth charts in current use.

In conclusion, the study has shown that there is a higher poverty in the Badia region and there was a tendency for boys in urban regions to be obese. Thus, by improving the socioeconomic conditions, family planning, health education regarding obesity and genetic education with regards to consanguinity, our children may grow better to achieve their genetic potentials for growth.

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The prevalence of hepatitis B carrier state in Khorassan province of Iran

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It was predicted that at least 400 million cases of hepatitis B chronic infection occurred by the year 2000 worldwide,[1] and now the figure has risen beyond this limit. According to the Center for Disease Control and Prevention (CDC) fact sheets, published on its website, hepatitis B infection has an acute case fatality rate of 0.5-1% and 2-10% of cases end up in chronic infection after 5 years. Premature mortality from chronic liver disease occurs in 15-25% of chronically infected persons, pointing to the importance of this global concern. In Iran, several studies have been performed to determine the prevalence of hepatitis B carrier state. In 1980s, almost 3% of population was affected, differing from a prevalence rate of 1.7% in Fars province to 5% in Sistan-Balouchestan province.[2] Fifty-one to 56% of Iranian cirrhotic patients were hepatitis B surface antigen (HBsAg) positive,[3,4] pointing to the importance of this infecting agent and its socio-economic burden in this country. With respect to the importance of this virus and its devastating consequences on society, for the first time in 1998, in a study that was performed in healthy population of Khorassan province, Iran, we tried to determine the prevalence of hepatitis B carrier state. Khorassan is the biggest province of Iran and it is located in the northeast.

This was a cross-sectional descriptive and quantitative study that was conducted on healthy population of Khorassan province in Iran in 1998. The subjects were in the age-range of 2-100 years from both genders. With regard to estimated prevalence of hepatitis B carrier state, a sample number of 4528 was considered to result in a meaningful outcome at the statistical significant level of 95%. According to the distribution of population, and based on the list of the places under the observation of the medical centers and traveling teams in rural areas and according to the list of the families who were vaccinated against poliomyelitis in 1996 in urban areas, the population under study was divided into 164 randomly selected sample clusters with 8 families in each cluster, 97 clusters were from urban and 67 clusters from rural areas. The data was obtained through completion of a questionnaire and taking blood samples, which were later examined in a medical laboratory in the center of province, detecting HBsAg by enzyme-linked immunosorbent assay (ELISA) method. We finally calculated the prevalence of carrier state in 100 patients

Table 1 - Number of hepatitis B surface antigen positive cases in each age group.

Age group (years)	Frequency of investigated people	Frequency of patients	n of cases per 100 people
2 - 10	1064	21	1.97
11 - 20	1217	35	2.87
21 - 30	751	34	4.52
31 - 40	552	33	5.97
41 - 50	362	13	3.59
51 - 60	226	7	3.09
61 - 70	217	7	3.22
71 - 80	122	13	10.65
81 - 90	13	0	0
91 - 100	4	0	0
Total	**4528**	**163**	

Table 2 - Marital status and location of patients

Marital status and locations	General population n (%)	HBsAg positive cases n (%)
Urban areas	2676 (59.1)	91 (55.8)
Rural areas	1852 (40.9)	72 (44.2)
Married (≥15 years)	(69)	103 (80.5)
Single (≥15 years)	(25.9)	20 (15.6)
Widowed (≥15 years)	(4.5)	5 (3.9)

HBsAg - hepatitis B surface antigen

in each age group and compared them with each other. The data was analyzed, using chi-square method and frequency tables to determine possible statistical relations by Statistical Package for Social Sciences software. Using ELISA method, HBsAg was positive in 163 cases (3.6%). Male patients constituted 51.5% (84 out of 163) and female patients 48.5% (79 of 163) of all patients, resulting in an almost equal male to female ratio. The prevalence of hepatitis B carrier state was similar in 2 genders (P=0.792). The average age of HBsAg positive cases was 31.67, with a medium of 29 years and mode of 24 years. In this study the youngest patient was a 2-year-old and the oldest was a 78-year-old. The largest number of cases was observed in the age range of 11-20 years, with 35 positive cases **(Table 1)** with most cases being within the age range of 20-40 years. Despite, the most prevalent age of carrier state was 71-80 years age group, with 10.65 patients in each 100 people **(Table 1).** A statistically significant difference in prevalence of carrier state in different age groups mentioned in **Table 1** was observed among our patients (P=0.000). **Table 2** demonstrates the marital status and locale of residence of our patients, there was no statistically significant difference in the place of residence and marital status of cases.

Depending on the prevalence of carrier state in a region, 3 levels of endemicity have been recognized for hepatitis B chronic infection. In high prevalence areas (≥8% of population affected), which constitutes 45% of global population, the lifetime risk of infection is >60% and early childhood infection is common. In intermediate prevalence areas (2-7%) which constitutes 43% of global population, the lifetime risk of infection is 20-60% and infection occurs in all age groups (CDC fact sheets). Middle-eastern countries except Kingdom of Saudi Arabia and Jordan have an intermediate prevalence rate. Iran has an intermediate prevalence of hepatitis B chronic infection, according to CDC. The prevalence of chronic carrier state in Iran had been reported to be 3% in 1980s.[5] The neonatal vaccination program launched in 1992 was not expected to change these figures for the general population before the year 2002. A recent study showed that the rate of hepatitis B carriers varied between zero and 3.9% with an average of 1.7%.[6] Therefore, it seems that currently CDC reports overestimate the rate of chronic infection in Iran. In this study, 3.6% of the population was HBsAg positive, putting Khorassan among the highly affected areas of Iran. With regard to the fact that the most common routes of transmission in this country have been prenatal transmission and intravenous drug abuse,[2] since the beginning of introduction of hepatitis B vaccine in "Expanded Program on Immunization" in Iran, it seems that the average age of the infected individuals have increased. When normalizing for the distribution of population, the highest prevalent age was 71-80 years age group in this study, demonstrating a significantly higher number of cases in comparison with other groups. In another study that was performed in different parts of Iran, older males living in a village with low socioeconomic status, poor sanitation and intrafamily contact were mostly infected.[6]

In this study, males and females were involved equally. Marital status and place of residence did not have any effect on distribution of carriers. Though, urban areas and married individuals were more affected with the infection. Our findings in this regard contrast the findings of previous studies on prevalence and socio-demographic distribution of cases.[6] By the way, results of studies about the mentioned factors are highly variable and this may result from differing socio-economic structure of a given location. For example, in two separate studies in Tanzania and Italy, no difference was observed in sexual prevalence of hepatitis B carrier state,[7,8] but in another study in Japan it has been more prevalent in males rather than females.[9]

Also, in Pellizzer et al[7] study in Tanzania, most of the cases were reported to be located in urban areas and in crowded families but in the study performed by Chiaramonte et al[8] in Italy, living area did not affect the prevalence rate of carrier state. To sum up, hepatitis B vaccination program and specific sociodemographic features of this region seem to have resulted in shifting up the average age of hepatitis B carrier state in Khorassan province. Although the most prevalent routes of transmission in Khorassan province have been prenatal and close household contact; further preventive measures aimed at this mainly young and middle aged population is needed to decrease the rate of disease propagation in society.

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Fine needle aspiration of the breast: A call for an organized service

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An outpatient fine needle aspiration (FNA) clinic at Prince Abdulrahman Al Sudairy Central Hospital, Sakaka Al-Jouf, Kingdom of Saudi Arabia (KSA), has been in place since 1994. The unit is performing FNA of the breast, thyroid, lymph-nodes, salivary gland masses, soft tissue masses and bone lesions. A pathologist takes FNAs, supervises the staining and reports on them. The majority of the cases are referred directly from the specialist clinics and are reported on the same day. Over a period of 8-years, expertise has been gained and FNA has become an integral part of the initial work-up of all superficial masses. During these 8 years (1994-2002), 276 women underwent FNA of the breast in this hospital. Their age ranged from 15-90 years with a mean of 42. Five reporting categories were used; 1. Inadequate, 2. Benign, here a diagnosis of specific condition was offered for example fibroadenoma, fat necrosis, duct ectasia, mastitis, if enough features were present to establish it with confidence, 3. Atypical hyperplasia, probably benign, 4. Suspicious, 5. malignant.

The FNA smears from 276 patients were reported as inadequate in 6.5 %, benign in 80%, atypical hyperplasia (probably benign) 1.5%, suspicious 0.7% and malignant in 11.3%. All the reported malignant cases (31) underwent definitive surgery either at our hospital or at tertiary referral centre where the FNA diagnoses was confirmed histologically. Thirty-two of the benign cases were operated and confirmed in the subsequent surgical biopsy. Thus, the sensitivity and specificity of FNA in detecting breast cancer in our series reached 100%. As a consequence to this success, the number of second operation (initial diagnostic biopsy followed by definitive surgery) on cancer bearing breast performed in this hospital was reduced by 73% in the first 4-years followed by 90.5% reduction in the next 4-years, after the introduction of FNA. In contrast to that, and over the same period of time, the benign to malignant ratio at open biopsy has increased from 5.5-17.6 and further to 30.5.

Our data demonstrated clearly the indisputable value of FNA in the diagnoses of breast lesions. The main purpose of FNA in the management of breast malignancy is to give a definitive pre-operative diagnosis that allows rapid referral or treatment, ideally in one operative session. This was achieved in all of our carcinoma cases. FNA is safe, rapid, repeatable and cost-effective. It leads to substantial savings in relation to the duration of hospital stay and operating room resources and time. It is an accepted fact that performance of FNA in the diagnoses of breast lesions improves with increased sensitivity and specificity over time.[1] Performed specifically by the pathologist, our inadequacy rate of 6.5% is among the lowest reported.[1] None of our cancer cases had inadequate FNA material. Inadequacy in our hospital was limited to benign cases only. Most of the inadequacy arose from patients with low clinical predictivity for malignancy who underwent FNA mainly for reassurance.

The excellence of our experience and its salutory effect on the management of most masses has been a source of great encouragement. We accordingly call for the

establishment of an effective organized FNA service all over KSA. An organized and efficient FNA service is needed in the KSA for several reasons. The incidence of cancer is increasing world wide. Most of the increase in cancer in the next 25-years is projected to occur in the developing countries, while incidence rates in industrial countries will remain stable or possibly decline, partly due to screening.[2] In KSA the reported breast cancer incidence is 14/100000.[3] It is bound to increase if the above anticipations are correct and FNA would contribute positively to the diagnosis and management. Unlike the findings in western countries, breast cancer in KSA presents late in relatively younger women.[4] Another important factor is that KSA is a very vast country, where thousands of kilometers separate between its major cities. In KSA, FNA is currently available mainly in tertiary centers and academic institutions. Whether it is present in regional and non-academic hospital is not known. The exact position of FNA in the management of breast diseases in these hospitals is also not known, as local experiences with FNA have not been published, except for a recent report from King Abdul-Aziz University Hospital in Jeddah, KSA.[5] Its availability in regional hospitals all over KSA would serve 2 main purposes: 1. It would ensure better management of breast cancer either through rapid referral to specialized centers or by offering a definitive treatment in one operative session where facilities are adequate, 2. It would allow expertise to be gained as a prelude to national screening program which is inevitable. This is important as FNA is the method of choice in early detection of cancer following suspicious mammography.

Establishment of FNA service would not impose any additional economic burden than is currently been born for the health need of the nation. Pathology Departments already exist in most secondary care hospitals. All that remains to achieve the service is the acquisition of well trained skilled personnel. This is of utmost importance as the outcome of FNA is operator dependent and errors in the diagnosis may lead to overtreatment or delays the diagnosis. Recruitment of such personnel should depend on documented experience supplemented by proficiency test. Appropriate guidelines to ensure uniform, standard and reliable service need to be written by a designated body or a committee. Such guidelines should include recommendations as to who are supposed to aspirate, how to prepare the material, adequacy requirements, reporting categories, criteria for evaluation and internal quality assurance. The performance of all laboratories should be closely monitored, and stringent external quality control measures have to be applied. Continuing education programs should be made available including workshops, conferences, courses and secondment to centers of expertise. As a base line, existing services should be encouraged to publish their results.

In this short communication, the importance of widespread, efficient and organized FNA breast service has been emphasized based on our experience in a secondary care hospital. The presence of such service would improve the management of breast cancer and ensure rapid referral to specialized centers. It would also be the very first step in a successful screening program.

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