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It was of great importance to publish a scientific journal by the ministry of public health & population. A Journal that is interested in researches & health medical studies that are carried out by Yemeni & other researchers in Yemen.

Goals / objectives ( purpose ) :-

1. Publishing health medical & researches, which are carried out by Yemeni researchers throughout free Journal, widely distributed among interest of health field personnel, in the institutes, facilities, Medical students, Medical schools teaching staffs, different Health institutes and other authorities.
2. Republish of Yemeni health & medical research which have been published in the international, regional journals and periodicals that are expensive and limited distribution in Yemen.
3. Encouraging Yemeni researchers to publish their researches & studies that have faced difficulties and complicated conditions and delay.
4. Collecting & documentation Yemeni health & medical research that published to be available as references for interested researchers and students.

Publication requirements:

1. Researches must be directly related to health & medical problems in Republic of Yemen.
2. Research must fulfill all methodological & ethical condition / regulations of scientific researches.
3. Arabic abstract should include the research paper if the original language of research in English.
4. Must not be more than five pages.
5. The journal is irresponsible in any way to the publishers.
Qat chewing and pesticides: a study of adverse health effects in people of the mountainous areas of Yemen

Junko Date¹, Noritoshi Tanida² and Tatsuya Hobara³

¹ Graduate School of Medicine, Yamaguchi University, Japan, ² Department of Medical Humanities, Yamaguchi University School of Medicine, Japan, ³ Department of Public Health, Yamaguchi University School of Medicine, Japan


Abstract:

Chewing qat leaves, Cathula Edulis, is now a very common behaviour among the people of the mountainous areas of Yemen. For about the past 20 years, in tandem with national development, qat chewing has been rapidly expanding, and the use of chemical pesticides in qat production has been increasing. In this study, the adverse effects on human health of qat chewing combined with pesticide use were investigated. Results of interviews and questionnaires showed that chewers of qat grown with few or no chemical pesticides and chewers of qat grown with chemical pesticides have considerably different subjective symptoms. Chewers of qat produced in fields where chemical pesticides are used regularly have more symptoms than chewers of qat produced in fields where chemical pesticides are rarely or never used. Chewers of qat produced with more chemical pesticides, in particular, experience acute adverse effects on the digestive system and chronic adverse effects such as body weakness and nasal problems. Farmers who chew homemade qat on which they spread chemical pesticides by themselves may have the highest health risks regarding the combination of qat and pesticides. It is concluded that chewing qat grown with chemical pesticides causes considerable adverse health effects in human beings.

Keywords: Yemen; qat; adverse health effects; subjective symptoms; pesticides.

Correspondence: Junko Date, c/o JICA TB Control Project, P. O. Box 17672, Sana’a, Republic of Yemen. Tel.: +967 – 1 – 412121; Fax: +967 – 1 – 414245; E-mail: jane@olive.freemail.ne.jp

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Introduction:

In the mountainous areas of northern Yemen, most men chew fresh qat leaves, Cathula Edulis, for several hours per day to enjoy the taste and to experience the stimulating effect on the nervous system. Kennedy et al. (1980) noted that 60% of men south of Sana’a were habitual qat users from 1955 – 1967, and the population of qat chewers was increasing at the time of the survey, from 1974 – 1976. Moreover, Weir (1985) noted qat was consumed regularly and frequently only by a wealthy minority of the Yemeni population until the 1970s. However, at present, it is difficult to find a man who does not chew qat, and most men chew approximately 100 – 300 g of qat leaves during continuous 3 – 6 h sessions every afternoon in Sana’a and the surrounding areas. This trend is related to increased qat production.

Increased qat production is linked to economic and social development at the national level. First, improved water management using irrigation has facilitated the cultivation of qat fields. Second, better mobile transportation on paved roads has contributed to the expansion of the qat market. Third, farmers prefer to produce and sell qat rather than other crops and fruits because there is no foreign competitor in the qat market. Finally, it has become easy to purchase foreign-made chemical products which can be used to grow large quantities of qat quickly. The area in which qat is cultivated in Yemen increased from 76,059 hectares in 1989 to 97,772 hectares in 1998, with 38.6% of the qat cultivation being in the Sana’a region in 1988. Moreover, the northern mountainous areas of Yemen, including Sana’a, are where most of the imported pesticides are used: 610.9 tons in 1992, or 93.6% of the total import (Ministry of Planning & Development and Ministry of Agriculture & Irrigation 2002 a). Figure 1 shows that the import of organic chemical products, including insecticides and fungicides, has been rapidly increasing since 1995. The Ministry of Agriculture and Fisheries (1987 a, b) has an official list of pesticides which are approved and forbidden for use. Guidelines for the safe use of pesticides were pusticised by the Ministry of Agriculture and Fisheries in 1984. However, in 2002, officials reported that pesticides were not used by farmers at the proper time and in the proper way (Ministry of Planning & Development and Ministry of Agriculture & Irrigation 2002 a). Qat – chewing behaviour has been accelerated by the cycle of expanding qat production, increased demand from chewers and increased economic benefits to local financial systems. The use of chemical pesticides contributes to this trend by sustaining the large quantity of qat available on a regular basis.
Scientifically, the main chemical constituents of qat, cathinone and methcathinone, stimulate the nervous system when they are absorbed through the mucus membrane; their concentrations in the blood peak 1 or 2 h after chewing and disappear after 6 h (Ministry of Planning & Development and Ministry of Agriculture & Irrigation 2002 b). Kennedy et al. (1983) noted that doctors whom they interviewed believed that use was not deleterious to the health, and they concluded, based on the results of their medical investigation, that medical case against qat use weak. However, 20 years later, Al-Motarreb et al. (2002 a) indicated that there was great awareness among Yemeni doctors regarding the effects of qat on general health and its effects on different diseases. It is noteworthy that chemical pesticides were rarely used by farmers in the 1980’s, in contrast to their frequent use now. The Ministry of Planning & Development and the Ministry of Agriculture & Irrigation (2002 b) noted that qat farmers resorted to pesticides to increase qat yields and improve qat quality. Recently, warnings about the health risks to human beings caused by both pesticides and qat have printed in the national newspaper (Al-Thawra 2002, 2003).

Fig1. Product area of qat, grape and coffee comparing with the import of chemicals from the year 1988-2001. (Source: Statistical Book from 2001 to 2002).
The adverse health effects of qat chewing were investigated by Hassan et al. (2002a); however, it is not clear whether these effects are caused by qat leaves only or by a combination of qat and pesticides. The focus of the current study is the adverse health effects of qat chewing, particularly in terms of pesticide use for the cultivation of qat. Although cases of acute pesticide poisoning associated with qat consumption have sometimes been reported in public, no clinical data regarding the chronic effects of pesticides associated with qat chewing are yet available. Thus, it is important to study both acute and chronic health effects that appear with the combination of pesticides and qat in order to distinguish these effects from the health effects of qat alone.

Methods:

The target population of the study was male residents of two different sites in mountainous areas near Sana’a. Male residents were chosen because the majority of men were expected to be qat chewers. The two investigation sites have different features. Area A is situated north of Sana’a city and has been a famous qat field for many years. Farmers in Area A contend that they use local soil as pesticides and very rarely use chemical pesticides. Pesticide specialists say the soil in certain places, such as Area A, contains sulphur (Ward 2000). Area B is situated west of Sana’a city, and production of qat has been developing for nearly 20 years. Farmers in Area B say they have utilized chemical pesticides since they started qat cultivation. Currently, they use Perfektion, the trade name of an organic phosphorous insecticide containing dimethoate (C5HI2NO3PS2), for qat fields in Area B. Dimethoate is certainly a very common commercial pesticide in Sana’a and the surrounding mountainous area according to the data collected during interviews in several commercial chemical product shops. The concentration of dimethoate pesticide residue in qat leaves was measured by gas chromatography in an authentic laboratory in Japan (Japan Food Research Laboratories, Tokyo).

In October 2003. Fresh qat leaves were purchased at the local qat market from Area A and Area B, the same location where the interview data were collected. These materials were transported to Japan. And the fresh qat leaves, in the same state used for chewing. Were extracted in acetone and concentrated on a rotary evaporator. The residue was re-dissolved in Dichioromethane and purified on a graphite carbon mini-column. The sample was dissolved in 10 ml acetone. These materials were analysed by gas chromatography using DB-5
column (J & W Scientific, Folsom, CA, USA). Dimethoate residue was measured in duplicate, and the average level was calculated. Three materials each from Area A and Area B were tested independently.

Information relative to the acute health effects of qat and pesticides was collected from June to July 2003 based on non-structured interviews with randomly selected residents of Areas A and B. The interviews took place at marketplaces where people come to purchase qat leaves every day. At the same time. These residents also responded to questionnaires about chronic health conditions. The total number of interviewees was 60 in Area A and 68 in Area B. All interviews and filling in of questionnaires were conducted in the Yemeni dialect of Arabic.

Statistical analysis of quantitative data was performed using Statistical Package for Social Science (SPSS) software. Logistic regression analysis was used in an effort to identify predictors of chronic adverse effects, and the non-parametric test was used for the analysis of each chronic subjective symptom. Statistical significance was set at two levels: $P < 0.05$ and $0.05 \leq P < 0.1$.

**Results :-**

**Chronic adverse health effects**

Out of a total of 128 respondents, 114 respondents, all qat chewers, completed the questionnaire (a response rate of 90.5 %). Table 1 shows the characteristics of the population in this study. All respondents were men who had never had any chronic disease diagnosed by medical doctors. Approximately 60 % of the respondents were farmers. Among samples of analysis for the 114 qat chewers, the median chewing frequency was 4 h per day. While filling out the questionnaire, the interviewees were asked to mark each symptom they had experienced frequently over a long period. Therefore, the subjective symptoms stated on the questionnaire imply chronic conditions and exclude temporary health conditions. The relationship of predictor variables and the existence of subjective chronic symptoms were tested by logistic regression analysis in Table 2. The results show a significant relationship between the existence of symptoms and the area of residence, either Area A or Area B. It is significant that 59.6 % of a total of 52 qat chewers in Area A had no symptoms, compared with only 19.4% of a total of 62 chewers in Area B ($P = 0.047$).
Table 1. Characteristics of the study population in this study, from June to July 2003

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total 114 qat chewers completed questionnaires n ( % )</th>
<th>Total 52 qat chewers in Area A n ( % )</th>
<th>Total 62 qat chewers in Area B n ( % )</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>114 (100 %)</td>
<td>52 (100 %)</td>
<td>62 (100 %)</td>
</tr>
<tr>
<td>Female</td>
<td>0 (0 %)</td>
<td>0 (0 %)</td>
<td>0 (0 %)</td>
</tr>
<tr>
<td><strong>Age (years)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- 19</td>
<td>5 (4.4 %)</td>
<td>5 (9.6 %)</td>
<td>0 (0 %)</td>
</tr>
<tr>
<td>20 – 29</td>
<td>42 (36.8 %)</td>
<td>18 (34.6 %)</td>
<td>24 (38.8 %)</td>
</tr>
<tr>
<td>30 – 39</td>
<td>36 (31.6 %)</td>
<td>17 (32.7 %)</td>
<td>19 (30.6 %)</td>
</tr>
<tr>
<td>40 -</td>
<td>31 (27.2 %)</td>
<td>12 (23.1 %)</td>
<td>19 (30.6 %)</td>
</tr>
<tr>
<td><strong>Education</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Illiterate</td>
<td>46 (40.4 %)</td>
<td>18 (34.6 %)</td>
<td>28 (45.1 %)</td>
</tr>
<tr>
<td>Literate or 9 years</td>
<td>32 (28.0 %)</td>
<td>11 (21.2 %)</td>
<td>21 (33.9 %)</td>
</tr>
<tr>
<td>9 years &lt;</td>
<td>36 (31.6 %)</td>
<td>23 (44.2 %)</td>
<td>13 (21.0 %)</td>
</tr>
<tr>
<td><strong>Occupation</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Farmers</td>
<td>67 (58.8 %)</td>
<td>29 (55.8 %)</td>
<td>38 (61.3 %)</td>
</tr>
<tr>
<td>Others</td>
<td>47 (41.2 %)</td>
<td>23 (44.2 %)</td>
<td>24 (38.7 %)</td>
</tr>
<tr>
<td><strong>Use of Chemical pesticides in farming</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>38 (33.3 %)</td>
<td>0 (0 %)</td>
<td>38 (61.3 %)</td>
</tr>
<tr>
<td>No</td>
<td>76 (66.7 %)</td>
<td>52 (100 %)</td>
<td>24 (38.7 %)</td>
</tr>
<tr>
<td><strong>Purchase of qat from local place always</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>114 (100 %)</td>
<td>52 (100 %)</td>
<td>62 (100 %)</td>
</tr>
<tr>
<td>No</td>
<td>0 (0 %)</td>
<td>0 (0 %)</td>
<td>0 (0 %)</td>
</tr>
<tr>
<td><strong>Average of chewing hours per day</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 2 hours</td>
<td>0 (0 %)</td>
<td>0 (0 %)</td>
<td>0 (0 %)</td>
</tr>
<tr>
<td>3 hours</td>
<td>45 (39.5 %)</td>
<td>21 (40.4 %)</td>
<td>24 (38.7 %)</td>
</tr>
<tr>
<td>4 hours</td>
<td>39 (34.2 %)</td>
<td>17 (32.7 %)</td>
<td>22 (35.5 %)</td>
</tr>
<tr>
<td>5 hours</td>
<td>17 (14.9 %)</td>
<td>9 (17.3 %)</td>
<td>8 (12.9 %)</td>
</tr>
<tr>
<td>6 hours</td>
<td>13 (11.4 %)</td>
<td>5 (9.6 %)</td>
<td>8 (12.9 %)</td>
</tr>
<tr>
<td><strong>Tobacco consumption</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Habitual users</td>
<td>76 (66.7 %)</td>
<td>24 (46.2 %)</td>
<td>52 (83.9 %)</td>
</tr>
<tr>
<td>Non – habitual users</td>
<td>38 (33.3 %)</td>
<td>28 (53.8 %)</td>
<td>10 (16.1 %)</td>
</tr>
</tbody>
</table>
All the respondents got qat either in the market of their own village or directly from their qat field. In Area A, 60% of respondents said they purchased locally produced qat from the particular sellers who produce qat without chemical pesticides.

The relationship of variables and the existence of subjective chronic symptoms is shown in Tables 3 and 4. In Area B, no significant difference was found between qat chewers who were farmers and those who were not. However, it is significant that 69.0% of a total of 29 qat chewing farmers had no symptoms in Area A, whereas 18.4% of a total of 38 qat-chewing farmers had no symptoms in Area B (P < 0.001).

In Area B, the top five subjective symptoms were lack of appetite, weakness, runny nose or congestion, headache and gingivitis (Table 5). As a result of the non-parametric analysis, significantly more interviewees in Area B than in Area A had ‘ weakness ’ ( P = 0.003 ), ‘ runny nose or congestion ’ ( P = 0.050 ) and ‘ change in hair color or loss of hair ’ ( P = 0.069 ).

Table 2. Relationship of predictor variables and existence of subjective chronic symptoms with 114 qat chewers.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Subjective symptoms</th>
<th>Number</th>
<th>More than one symptom</th>
<th>None</th>
<th>P value (Logistic Regression)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- 19</td>
<td>5</td>
<td>4</td>
<td>1</td>
<td></td>
<td>0.821</td>
</tr>
<tr>
<td>20 – 29</td>
<td>42</td>
<td>27</td>
<td>15</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30 – 39</td>
<td>36</td>
<td>19</td>
<td>17</td>
<td></td>
<td></td>
</tr>
<tr>
<td>40 –</td>
<td>31</td>
<td>21</td>
<td>10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Residential area</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A area</td>
<td>52</td>
<td>21</td>
<td>31</td>
<td></td>
<td>0.047</td>
</tr>
<tr>
<td>B area</td>
<td>62</td>
<td>50</td>
<td>12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Illiterate</td>
<td>46</td>
<td>26</td>
<td>20</td>
<td></td>
<td>0.501</td>
</tr>
<tr>
<td>Literate or ≤ 9 years</td>
<td>32</td>
<td>24</td>
<td>8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9 years &lt;</td>
<td>36</td>
<td>21</td>
<td>15</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Occupation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Farmers</td>
<td>67</td>
<td>40</td>
<td>27</td>
<td></td>
<td>0.283</td>
</tr>
<tr>
<td>Others</td>
<td>47</td>
<td>31</td>
<td>16</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tobacco consumption</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>76</td>
<td>50</td>
<td>26</td>
<td></td>
<td>0.879</td>
</tr>
<tr>
<td>No</td>
<td>38</td>
<td>21</td>
<td>17</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 3. Relationship of variables and the existence of subjective chronic symptoms with 62 qat chewers in Area B.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Number</th>
<th>More than one symptom</th>
<th>None</th>
<th>P value (Logistic Regression)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Occupation</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Farmers</td>
<td>38</td>
<td>31</td>
<td>7</td>
<td>0.926</td>
</tr>
<tr>
<td>Others</td>
<td>24</td>
<td>19</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td><strong>Tobacco occupation</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>52</td>
<td>42</td>
<td>10</td>
<td>0.991</td>
</tr>
<tr>
<td>No</td>
<td>10</td>
<td>8</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td><strong>Average of chewing hours per day</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 2 hours</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0.361</td>
</tr>
<tr>
<td>3 hours</td>
<td>24</td>
<td>21</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>4 hours</td>
<td>22</td>
<td>17</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>5 hours</td>
<td>8</td>
<td>6</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>6 hours</td>
<td>8</td>
<td>6</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

Table 4. Relationship of variables and the existence of subjective chronic symptoms of 114 qat chewers regarding farmers and non-farmers.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Number</th>
<th>More than one symptom</th>
<th>None</th>
<th>P value (Logistic Regression)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Farmers</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A area</td>
<td>29</td>
<td>9</td>
<td>20</td>
<td>0.000</td>
</tr>
<tr>
<td>B area</td>
<td>38</td>
<td>31</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td><strong>Other occupation</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A area</td>
<td>23</td>
<td>12</td>
<td>11</td>
<td>0.049</td>
</tr>
<tr>
<td>B area</td>
<td>24</td>
<td>19</td>
<td>5</td>
<td></td>
</tr>
</tbody>
</table>

In Area A, one of the places famous for qat production, most farmers contended that they never use chemical pesticides. In Area B, farmers said that they have been using chemical pesticides since they began cultivating the area for qat production. Currently, they use dimethoate. From the results of the laboratory examination, the average dimethoate residue in the qat from Area A is $3.23 \pm 0.125$ ppm (mean \pm SD), while that from Area B is $14.7 \pm 0.47$ ppm (mean \pm SD).
Acute adverse health effects

From the interviews conducted in both areas, it was found that qat chewers sometimes complained about acute adverse effects of qat, such as a lack of appetite just after chewing qat, insomnia at night and a dull feeling in the morning. However, they said qat caused no health problems and they were always well when they start chewing qat every afternoon.

Moreover, the interviewees in Area B had much more information about the relationship between chemical pesticides and health than the interviewees in Area A had. Most of the interviewees in Area B said they had experienced ‘bad effects from chemicals’ such as dizziness, headache, stomach ache, stomach bulge and vomiting.

On 10 January 2002, the Yemeni daily newspaper, Al-thawra, reported a case of poisoning by pesticide-laden qat:-

A 29 – year – old man died after chewing qat. He had symptoms of toxicity, including heavy vomiting and diarrhea. Similar cases had been reported during the winter. The reason for the poisoning cases is that farmers followed the wrong procedure for chemical use. They did not wait the necessary interval after spreading chemical powder onto qat trees, and they harvested the qat too soon.

One interviewee in Area B expressed a remarkable opinion concerning the above incident:-

Such a poisoning case is an accident (Haadith in Arabic), but not an illness (marad in Arabic). Chewing qat is not a problem, but chewing qat remaining chemicals may become a problem because chemicals are poisons. Farmers use chemicals just before the qat harvest. If no rain washes these chemicals away farmers quickly harvest the qat leaves, chemical poisons remain on the leaves. Therefore, we must wash the leaves with water. If we do so, we will never have a chemical poisoning accident. At the same time, we cannot escape taking in chemicals whenever we chew qat. Every farmer uses chemicals on qat. We want to chew qat; thus, we buy qat. Is there any other choice? Wash qat before chewing. This is the solution.

Although most of the interviewees in Area B experienced ‘bad effects from chemicals,’ they contended the effects were avoidable if they washed the qat leaves. The fact is that when dimethoate, an organic phosphorus pesticide, is used, the chemical components cannot be removed from the surface of the qat leaves by water because they permeate the tissues.
Table 5. Subjective chronic symptoms of qat chewers in Area A and B

<table>
<thead>
<tr>
<th>Subjective symptoms</th>
<th>Area A (n = 52)</th>
<th>Area B (n = 62)</th>
<th>P value (Non-parametric)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lack of appetite</td>
<td>7</td>
<td>17</td>
<td>0.105</td>
</tr>
<tr>
<td>Weakness</td>
<td>3</td>
<td>17</td>
<td>0.003 a</td>
</tr>
<tr>
<td>Nose running or stopping up</td>
<td>5</td>
<td>15</td>
<td>0.050 b</td>
</tr>
<tr>
<td>Headache</td>
<td>3</td>
<td>10</td>
<td>0.137</td>
</tr>
<tr>
<td>Gingivitis</td>
<td>5</td>
<td>9</td>
<td>0.569</td>
</tr>
<tr>
<td>Decayed tooth</td>
<td>11</td>
<td>8</td>
<td>0.314</td>
</tr>
<tr>
<td>Colic</td>
<td>5</td>
<td>8</td>
<td>0.769</td>
</tr>
<tr>
<td>Difficult breathing</td>
<td>3</td>
<td>7</td>
<td>0.341</td>
</tr>
<tr>
<td>Joint – ache or backache</td>
<td>4</td>
<td>7</td>
<td>0.542</td>
</tr>
<tr>
<td>Dizziness</td>
<td>6</td>
<td>7</td>
<td>1.000</td>
</tr>
<tr>
<td>Cough</td>
<td>3</td>
<td>7</td>
<td>0.341</td>
</tr>
<tr>
<td>Changed color of hair, or loss of hair</td>
<td>1</td>
<td>7</td>
<td>0.069 b</td>
</tr>
<tr>
<td>Weight loss (thinness)</td>
<td>3</td>
<td>6</td>
<td>0.506</td>
</tr>
<tr>
<td>Nervousness</td>
<td>4</td>
<td>6</td>
<td>0.753</td>
</tr>
<tr>
<td>Lot of sweat</td>
<td>2</td>
<td>5</td>
<td>0.452</td>
</tr>
<tr>
<td>Feeling tired</td>
<td>5</td>
<td>5</td>
<td>1.000</td>
</tr>
<tr>
<td>Laryngitis</td>
<td>2</td>
<td>5</td>
<td>0.452</td>
</tr>
<tr>
<td>Tears</td>
<td>2</td>
<td>4</td>
<td>0.687</td>
</tr>
<tr>
<td>Sleeplessness</td>
<td>0</td>
<td>3</td>
<td>0.249</td>
</tr>
<tr>
<td>Diarrhea or constipation</td>
<td>4</td>
<td>3</td>
<td>0.700</td>
</tr>
<tr>
<td>Changed color of Skin</td>
<td>2</td>
<td>3</td>
<td>1.000</td>
</tr>
<tr>
<td>Allergy</td>
<td>2</td>
<td>3</td>
<td>1.000</td>
</tr>
<tr>
<td>Vomiting or nausea</td>
<td>2</td>
<td>1</td>
<td>0.591</td>
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<tr>
<td>Hand shaking</td>
<td>1</td>
<td>1</td>
<td>1.000</td>
</tr>
<tr>
<td>Buzzing in ears</td>
<td>4</td>
<td>1</td>
<td>0.176</td>
</tr>
<tr>
<td>Cracked or color changed of nail</td>
<td>3</td>
<td>0</td>
<td>0.092 b</td>
</tr>
<tr>
<td>Heart problem</td>
<td>1</td>
<td>0</td>
<td>0.456</td>
</tr>
<tr>
<td>Swelling</td>
<td>0</td>
<td>0</td>
<td>1.000</td>
</tr>
</tbody>
</table>

Mark ‘a’ indicates the difference (P < 0.05) between Areas A and B.
Mark ‘b’ indicates the difference (0.05 ≤ P < 0.1) between Areas A and B.
Discussion:

Hassan et al. (2002a) noted that qat chewing induces anorexia, a weak stream of micturition, post-chewing urethral discharge and insomnia. Moreover, there have been several reports on the relationship between qat chewing and acute myocardial infarction (Al-Motarreb et al. 2002b), anxiety and depression (Hassan et al. 2002b), haemorrhoidal disease (Al-Hadrani 2000), duodenal ulcer (Raja’a et al. 2000) and squamous cell carcinoma (Nasr and Khatri 2000). These articles mention adverse effects of qat alone. However, in the current study, some interviewees in Area B stressed that adverse health effects were caused by qat combined with chemicals. The problems they noted were dizziness, headache, stomach ache, stomach bulge and vomiting. Naito (2001) stated the particular toxic symptoms from organic phosphorus insecticides, including dimethoate, are weakness, nausea, headache, colic and dizziness. It is possible that complaints of chewers in Area B about acute adverse effects were related to pesticides, not to qat alone.

Dimethoate is moderately toxic by ingestion, inhalation and dermal absorption. Severe dimethoate poisoning affects the central nervous system, causing such symptoms as lack of coordinathoate, slurred speech, loss of reflexes, weakness, fatigue, involuntary muscle contractions and twitching. Repeated or prolonged exposure may result in the same effects as acute exposure (Pesticides News 2002). FAO/WHO reported that, based on toxicological evaluations, the level causing no toxicological effect for a man is 0.2 mg kg\(^{-1}\) body weight per day and the estimated acceptable daily intake for a man (ADI) is 0.002 mg kg\(^{-1}\) body weight (JMPR 1996). The amount of dimethoate residue of qat in Area A was 3.23 ppm, and that of Area B was 14.7 ppm. Assuming that the average body weight of Yemeni man is 60 kg and daily qat intake is 100 mg, which is that minimum quantity commonly used, the daily intake of dimethoate of Area A is 0.323 mg and that of Area B is 1.47 mg, whereas the ADI should be 0.12 mg. Even if some of residue may be deducted because chewers at last spit the remains of qat out of mouth, the pesticide residue of qat in Area B is quite considerable. The fact that the level of dimethoate residue in Area B is approximately five times higher than that of Area A conforms to the analysis of interviews and questionnaires, indicating that qat chewers in Area B have more acute and chronic adverse health effects. While the level causing no toxicological effect is 12 mg for a person weighing 60 kg, fatal effects could occur from daily consumption in rare cases. However...
it should be noted here that farmers contended that they used more pesticides in winter; thus, more pesticide residue may remain in qat in winter, January to February, than remained in the qat which were purchased and examined in October.

In biological tests using mice, Thabet (2000) investigated the effects of qat combined with insecticides. After oral administration of a combination of dimethoate and ethanol qat extract, he concluded that the combination is significantly more antagonistic to both acetyl cholinesterase and monoamine oxidase activities in the brain and heart of mice than the ethanol qat extract alone. Qat leaves pharmacologically act as an amphetamine, stimulating the sympathetic nerves. The Thabet report implies that qat with dimethoate has much stronger effects on the sympathetic nervous system than qat alone. It is suggested that, as in the case of the mice, adverse health effects in human beings are also enhanced by chewing qat combined with pesticides.

At present, there is little concern regarding chronic health problems caused by the combination of qat and pesticides, and no investigation or report has been published regarding pesticide residue in qat. From the current study, though, chronic adverse health effects can be predicted. Compared with the people in Area A, who chew qat produced with little or no dimethoate, the people in Area B, who chew qat produced with more dimethoate, have considerably more health problems. Weakness had been noted as a temporary qat-related public health problem; however, here it is clear that many more chewers of qat produced with chemicals have these symptoms chronically than do chewers of qat produced with fewer chemicals. Nasal problems are also considered to be a particular chronic health problem among chewers of qat produced with chemical pesticides.

It is noteworthy that farmers in Area B have significantly more health problems than farmers in Area A. Farmers who chew qat that raise themselves using pesticides may be at high risk not only because of oral consumption of qat with pesticides but also because of their work spreading pesticides on the field. In contrast, farmers who produce qat using fewer chemical pesticides avoid both the occupational risk and consumption risk of chemically produced qat. Alternatively, as shown in Table 3, farmers and other workers in Area B have similar risk levels for health problems, which implies that the major cause of adverse effects may be the oral intake of qat and dimethoate rather than the inhalation or dermal absorption of dimethoate in farming. At least, it may be
considered that the group at highest risk for chronic health problems is farmers who work with chemical pesticides on qat trees and chew their qat regularly.

**Conclusion:**

Qat chewing is now very common among the people of the mountainous areas of Yemen. Results show that acute adverse health effects, such as a bulging stomach and stomach ache, are common among chewers of qat produced with chemical pesticides and that chronic adverse health effects, such as weakness and nasal problems, are also claimed by chewers of chemically produced qat. These health problems are not caused by only chewing qat grown with chemical pesticides such as dimethoate. Thus, it is concluded that the use of chemical pesticides on qat leaves strengthens the adverse effects on human health.

In particular, farmers who use chemical pesticides on qat trees and chew their qat leaves at highest risk for health problems related to qat and pesticides.

**Acknowledgements:**

The authors are grateful to Naoya Takada, Graduate School of Agricultural and Life Sciences, the University of Tokyo, for his advice from the viewpoint of agricultural economics. The authors appreciate Yahya Ali Mudhaffar and Faisal As-Shaaws for their assistance with quantitative data collection. The authors are also grateful to the Ministry of Public Health in Yemen for its support of this research and to the people who granted interviews.

**Reference :-**


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PREVALENCE OF THE SICKLE CELL GENE IN YEMEN: A PILOT STUDY

Authors:

Hafiz Al-Nood1, * Saad Al-Ismail1, Lawrence King2 and Alison May3

1 Clinical School, University of Wales Swansea, Singleton Park, Swansea, UK.
2 Departments of Haematology, Llandough Hospital, Penarth, Cardiff, UK.
3 Departments of Haematology, University of Wales College of Medicine, Heath Park, Cardiff, UK.


Abstract:

To determine the prevalence of the sickle cell gene (βs) in Yemen and amongst people from different regions of the country living in the capital, Sana’a City, cord blood samples from 1,500 consenting mothers were collected from hospitals in Sana’a City between July and December 2001. The names and original homes of the parents were recorded. Cation exchange high performance liquid chromatography (HPLC) analysis was used for screening, while isoelectric focusing (IEF) and DNA polymerase chain reaction (PCR) were used to confirm Hb S [β6 (A3) Glu → Val]. Thirty-three samples were found to show Hb FAS, giving an overall likely βs gene frequency of 0.011. The βs gene frequency varied with the part of the country from which the parents came. Amongst people from Taiz and Haja in the west, the gene frequency was more than 0.04, but less than 0.004 amongst people from Ibb, adjacent to the governorate (administrative division) of Taiz. Of 66 chromosomes from babies carrying the Bs gene, only 1.5% also carried the 158 (C → T) Gγ-globin gene XmnI site compared with 16.1% of 168 chromosomes from babies without the βs gene from the same regions.

* Correspondence: Mr. Hafiz Al-Nood, Clinical School, University of Wales Swansea, Singleton Hospital, Singleton Park, Sketty, Swansea SA2 8QA, Wales, UK; E-mail: Hafizalnood@Yahoo.co.uk.

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The results of this study thus show a higher $\beta^s$ gene frequency in the western coastal part of Yemen than in the central mountainous and eastern desert areas. The incidence of affected homozygous births May therefore reach 20/10,000 in certain areas, although it is much lower than this overall. Limited health resources can best be invested in developing a program of education, screening and health care, initially prioritizing those communities residing in the western areas of Yemen with the highest $\beta^s$ gene frequency.

**Key words:** Yemen; sickle cell; Hemoglobinopathies.

**Introduction:**

The mutation giving rise to Hb S, the cause of sickle cell disorders, is a $\text{GAG} \rightarrow \text{GTG}$ transversion in the second residue of codon 6 of the $\beta$-globin gene, resulting in the replacement of glutamic acid by valine (1). This mutation is linked to different $\beta$-globin gene haplotypes. Certain haplotypes such as the Arab-India $\beta^s$-linked haplotype, carry the $–158 (\text{C} \rightarrow \text{T}) \text{XmnI}$ polymorphism in the $G$-$\gamma$-globin gene promoter that is predominant in the eastern region of Saudi Arabia where the condition is mild (2).

Yemen is located on the southwest corner of the Arabian Peninsula and has a population of about 18 million (3). Previously reported values for $\beta^s$ prevalence amongst Yemeni people have been obtained by studying those people who have migrated elsewhere and so may not accurately reflect the true situation in the Yemen (4, 5). For instance, White et al. (5) found the gene frequency among 1.260 Yemeni in Abu Dhabi, United Arab Emirates (UAE), to be 0.005. Determination of the prevalence of the $\beta^s$ gene in Yemen is essential for assessing its role in childhood mortality and morbidity, and the health care resources needed to address the impact of the disease on its population. It was therefore decided to conduct a pilot study of the indigenous Yemen population that would give some indication of overall prevalence, as well as the likely distribution of prevalences over the various governorates (administrative divisions). At the same time, it was hoped to explore the best approach and technologies required for extending the study to obtain more accurate data.
Materials and Methods:

Samples:

Between July to December 2001, a total of 1,500 cord blood samples were collected in EDTA from Yemeni newborns whose mothers had given their verbal consent in the maternity departments at Al-Sabain Hospital, Al-Thawra Hospital, Al-Kuwait Hospital and Mother Hospital in Sana’a City, Yemen. The names and residential origins of parents were also recorded. Cord blood samples were put on Guthrie cards (Schliecher and Schuell, The Science and Art Company, batra GmbH, Traben-Trabach, Germany) within 24 hours of collection, and these were kept at 4°C during storage and transportation to the UK. The samples were subsequently analysed at the Cardiff Sickle Cell and Thalassaemia Laboratory located in Llandough Hospital and the University Hospital of Wales, Cardiff, Wales, UK.

High Performance Liquid Chromatography:

A cation exchange high performance liquid chromatography (HPLC) system (Shimadzu, Kyoto, Japan) and an optimized gradient of a β-thalassaemia (that) test kit (Chromsystems Instruments & Chemicals, GmbH, Munich, Germany) were used to analyze all the samples for Hbs A, F, S, C and D. Samples were prepared for analysis by punching out a 6 mm diameter portion of the blood spot on the Guthrie card and eluting the haemoglobin (Hb) with 1 ml haemolysis reagent (Chromsystems Diagnostics) for 15 min. continuous mixing (6).

Isoelectric Focusing:

Isoelectric focusing (IEF) on agarose gels (Resolve System, Haemoglobin test kit; Perkin Elmer Life Sciences, Norton, OH, USA) was used to confirm Hb variants such as Hb S detected by HPLC. A 6 mm disc from each dry blood spot sample was eluted in 50 μL Hb elution solution supplied by Perkin Elmer for 15 min. of continuous mixing. Then the samples were focused on agarose gels for 90 min. at 1.5 kV, 18 mA, after which the protein was fixed by immersion in 5% trichloracetic acid in 35% methanol and the plate was dried at 50 to 60°C (7).
Extraction of DNA :

DNA was extracted from the Guthrie card by adding 60 µL buffer for EDTA blood ( Applied BioSystems, Foster City, CA, USA) to a 5 mm diameter portion of the blood spot on the Guthrie card as per the manufacturer’s instructions. This was incubated at 97°C for 40 min., centrifuged and the buffered supernatant transferred to a clean tube.

Determination of βS and Other β-Globin Gene Mutations:-

The βS mutation was detected by a previously published method involving polymerase chain reaction ( PCR ) amplification of first two exons of the β-globin gene followed by DdeI digestion of the PCR product (8). Further mutation analysis of the β-globin gene coding region was carried out by PCR amplification of the first two exons of the β-globin gene using the forward primer 5’-GGC CAA TCT ACT CCC AGG AG-3’ and the reverse primer 5’-ACA TCA AGG GTC CCA TAG AC-3’, and PCR amplification of the third exon of the β-globin gene using the forward primer 5’-CAA TGT ATC ATG CCT CTT TGC ACC-3’ and the reverse primer 5’-CAC TGA CCT CCC ACA TTC CC-3’, followed by direct sequence analysis using the same primers and the ABI PRISM™ BigDye fluorescent dideoxy chain terminator cycle sequencing kit ( Applied BioSystems ). The fluorescent products were separated by capillary electrophoresis and analyzed using an ABI 3100 Genetic Analyser (Applied BioSysstems).

Determination of the –158(C → T) Gγ-gamma Globin Gene XmnI Polymorphism:-

The –158 ( C→T ) Gγ-globin gene XmnI polymorphism was detected by PCR amplification using 5’-GAA CTT AAG AGA TAA TGG CCT AA-3’ and 5’-ATG ACC CAT GGC GTC TGG ACT AG-3’ as forward and reverse primers respectively (9), followed by digestion of the PCR product with the restriction endonuclease XmnI ( New England Biolabs Inc., Beverly, MA , USA ) . Digested fragments were separated on agarose gelelectrophoresis and analyzed after ethidium bromide staining. The-158 ( C → T ) creates a restriction site for this enzyme and digested fragments of 420 and 220 bp are observed.

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Figure 1. High performance liquid chromatography elution: (a) sample showing no abnormalities; (b) sample from a baby found to have Hb AS; (c) sample Al-Thawra 402; (d) sample Al-Sabain 1771; (e) sample Al-Thawra 2; (f) sample Al-Sabain 1203.
Prevalence of beta-S:-

The overall prevalence of sickle cell trait was calculated as the percentage of sickle cell trait samples detected amongst the total tested. Prevalence for different localities was determined indirectly, from the information on the places of residence of the parents. If the parents were from different governorates that child was considered as come from either one or the other, and lower and upper limits for prevalences for these areas are therefore given.

RESULTS:

High Performance Liquid Chromatography:-

Of the total 1,500 cord blood samples analysed by HPLC, all chromatograms showed peaks eluting in the positions of Hb A and Hb F (Figure 1). Although no samples showed obvious signs of maternal blood contamination (adult Hb>50% and a definite HbA2 peak), 40 samples (2.7%) showed Hb A2 >0.5% and adult Hb>20% which we decided empirically could indicate the additional presence of maternal blood. This was higher than expected but is not thought to have had a major effect on the conclusions drawn from this pilot study. Thirty-eight samples showed abnormal haemoglobin peaks. Thirty-four of these had peaks in the position of HbS (Figure 1b) one of which (sample Al-Kuwait 59) was unusually small and of uncertain significance.

The sample Al-Thawra 402 showed a peak between Hb F and Hb A and a minor peak in the Hb A2 position. Sample Al-Sabain 1771 showed two peaks, one between Hb A and Hb A2 and a minor peak eluting later than Hb S. Sample Al-Thawra 2 showed a single extra peak between Hb A and Hb F, and sample Al-Sabain 1203 showed a single peak between Hb A and Hb A2 (Figure 1c- f ).

Figure 2. Isoelectric focusing plate. Lane 1: Al-Thawra 402. Lane 2: Control ASC. Lane 3: Sickle cell trait. Lane 4: Al-Sabain 1771. Lane 5: Sickle cell trait. Lane 6: Normal. Lane 7: Al-Thawra 2. Lane 8: Normal. Lane 9: Sickle cell trait. Lane 10: Al-Sabain 1203. Lane 11: Sickle cell trait.

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Lane 12: Sickle cell trait. Lane 13: Control ASC.

Isoelectric Focusing:

Thirty-three of the samples, showing abnormal haemoglobin peaks on HPLC, were confirmed by IEF as probable Hb FAS (Figure 2). The sample Al-Kuwait 59 showed no variant haemoglobin band at all and was confirmed to lacking the beta-S mutation by DNA studies.

Table 1. The hospitals from which the blood samples found to contain variant haemoglobins were collected and the place of origin of each parent.

<table>
<thead>
<tr>
<th>Number</th>
<th>Hospital</th>
<th>Sample number</th>
<th>Mother's place of origin</th>
<th>Father's place of origin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb FAS 1</td>
<td>Mother</td>
<td>9</td>
<td>Taiz</td>
<td>Sanaa</td>
</tr>
<tr>
<td>2</td>
<td>Al-Sabain</td>
<td>1046</td>
<td>Taiz</td>
<td>Taiz</td>
</tr>
<tr>
<td>3</td>
<td>Al-Sabain</td>
<td>1144</td>
<td>Sanaa</td>
<td>Sanaa</td>
</tr>
<tr>
<td>4</td>
<td>Al-Sabain</td>
<td>1194</td>
<td>Taiz</td>
<td>Taiz</td>
</tr>
<tr>
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<td>Al-Sabain</td>
<td>1217</td>
<td>Sanaa</td>
<td>Sanaa</td>
</tr>
<tr>
<td>6</td>
<td>Al-Sabain</td>
<td>1238</td>
<td>Haja</td>
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<tr>
<td>7</td>
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<td>1300</td>
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<td>Taiz</td>
</tr>
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<td>Taiz</td>
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<td>1732</td>
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<td>69</td>
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<td>Al-Mahweet</td>
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<td>Al-Thawra</td>
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<td>Sanaa</td>
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<td>33</td>
<td>Al-Thawra</td>
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<td>Sanaa</td>
<td>Sanaa</td>
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<td>Hb FA?34</td>
<td>Al-Sabain</td>
<td>1203</td>
<td>Ibb</td>
<td>Ibb</td>
</tr>
<tr>
<td>35</td>
<td>Al-Sabain</td>
<td>1771</td>
<td>Al-Beida</td>
<td>Al-Beida</td>
</tr>
<tr>
<td>36</td>
<td>Al-Thawra</td>
<td>2</td>
<td>Al-Mahweet</td>
<td>Al-Mahweet</td>
</tr>
</tbody>
</table>

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DNA Studies:-

All 33 samples showing a peak in the Hb S window on HPLC and a band in the HbS position on IEF were confirmed as heterozygous Hb S by the loss of the DdeI restriction enzyme site. Direct sequence analysis of all three β globin gene exons of the four samples containing unknown haemoglobin variants revealed an abnormality only in sample Al-Sabain 1203 which showed heterozygosity for an adenine to cytosine substitution at codon 22 (GAA→GCA). This predicts the replacement of alanine by glutamic acid, which occurs in Hb G Coushatta [β22(B4) Glu – Ala] (10).

Prevalence of beta-S:-

Table 1 shows the places of origin of the parents of the children tested and found to have haemoglobin variants. Figure 3 show the distribution of sickle cell trait and total collected number of sample in each governorate of Yemen. No beta-S homozygotes were detected in this study.

![Distribution of sickle cell trait and total collected number of sample in each governorate of Yemen](image)

Table 2 shows the calculated beta-S gene frequencies. The beta-S gene frequency was predicted to be highest (probably >0.01) in the following governorates: Haja: 0.003 to 0.050, Taiz: 0.038 to 0.044, Al-Hodeidah: 0.019 to 0.037, Amran: 0.023. The governorates of Sanaa and Sanaa City, Ibb,
Dhamar, Al-Baida and Al-Mahweet appear to have lower (probably <0.01) beta-S gene frequencies.

**Prevalence of the -158 (C→T) G-gamma Globin Gene XmnI Polymorphism :-**

Only one of the 66 chromosomes (1.5%) from the samples indicating sickle cell trait (Hb FAS) showed the presence of the G-gamma globin gene promoter XmnI site, i.e. 3.0% maximum of the beta-S chromosomes, compared with 27 (16.1%) of the 168 chromosomes from Hb FA samples carefully selected from the same governorates as the Hb FAS samples. The beta-S mutation in Yemen is therefore not usually on the Arab-Indian haplotype that is associated with a milder clinical course.

Table 2. The prevalence of sickle cell trait in different governorates of Yemen

<table>
<thead>
<tr>
<th>Governorate</th>
<th>Investigated sample number</th>
<th>Prevalence Hb(AS)(^a)</th>
<th>Haemoglobin S gene frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number</td>
<td>%</td>
<td></td>
</tr>
<tr>
<td>Sanaa&amp;Sanaa City</td>
<td>745</td>
<td>10-12(^b), 1.34-1.61%</td>
<td>0.007-0.008</td>
</tr>
<tr>
<td>Aden</td>
<td>18</td>
<td>0, 0.0</td>
<td></td>
</tr>
<tr>
<td>Taiz</td>
<td>171</td>
<td>13-15(^b), 7.6-8.77%</td>
<td>0.038-0.044</td>
</tr>
<tr>
<td>Al-Hodeidah</td>
<td>27</td>
<td>1-2(^b), 3.7-7.4%</td>
<td>0.019-0.037</td>
</tr>
<tr>
<td>Laheg</td>
<td>1</td>
<td>0, 0.0</td>
<td></td>
</tr>
<tr>
<td>Ibb</td>
<td>179</td>
<td>1, 0.56%</td>
<td>0.003</td>
</tr>
<tr>
<td>Abyan</td>
<td>13</td>
<td>0-1(^b), 0.0-7.69%</td>
<td>IS(^c)</td>
</tr>
<tr>
<td>Dhamar</td>
<td>138</td>
<td>0-1(^b), 0.0-0.73%</td>
<td>0.000-0.004</td>
</tr>
<tr>
<td>Shabwah</td>
<td>2</td>
<td>0, 0.0</td>
<td></td>
</tr>
<tr>
<td>Haja</td>
<td>30</td>
<td>2-3(^b), 6.67-10%</td>
<td>0.033-0.050</td>
</tr>
<tr>
<td>Al-Baida</td>
<td>53</td>
<td>0-1(^b), 0.0-1.9%</td>
<td>0.000-0.009</td>
</tr>
<tr>
<td>Hadramout</td>
<td>16</td>
<td>0, 0.0</td>
<td>IS(^c)</td>
</tr>
<tr>
<td>Saadah</td>
<td>4</td>
<td>0, 0.0</td>
<td>IS(^c)</td>
</tr>
<tr>
<td>Al-Mahweet</td>
<td>45</td>
<td>0-1(^b), 0.0-2.22%</td>
<td>0.000-0.011</td>
</tr>
<tr>
<td>Al-Mahrah</td>
<td>1</td>
<td>0, 0.0</td>
<td>IS(^c)</td>
</tr>
<tr>
<td>Mareb</td>
<td>16</td>
<td>0, 0.0</td>
<td>IS(^c)</td>
</tr>
<tr>
<td>Al-Jawf</td>
<td>4</td>
<td>0, 0.0</td>
<td>IS(^c)</td>
</tr>
<tr>
<td>Amran</td>
<td>22</td>
<td>1, 4.55%</td>
<td>0.023</td>
</tr>
<tr>
<td>Al-Dach</td>
<td>15</td>
<td>0, 0.0</td>
<td>IS(^c)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>1,500</td>
<td>33, 2.2%</td>
<td>0.0110</td>
</tr>
</tbody>
</table>

\(^a\) No beta-S homozygotes were found.
b The infant has parents who come from different governorates and the beta-S gene is forming one or the other.

c insufficient samples for frequency estimation.

**DISCUSSION:**

Sickle cell disorders are amongst the most prevalent genetic diseases. This study shows that 2.2% cord bloods collected in various hospitals of the capital city of Yemen showed a haemoglobin composition consistent with being from babies with sickle cell trait. Sickle cell disorders are therefore likely to be a health problem for the people of Yemen. Despite the low number of samples studied per area, it is clear that Yemen has different beta-S gene frequencies in different governorates and likely carrier rates of 7.6% to 8.8%, and 6.6% to 10% were observed amongst babies whose parents were from Taiz and Haja, respectively. It is estimated that the annual number of malaria cases in Yemen is around 3 million (11), and the highest beta-S gene frequency was found in samples from the endemic area of malaria that is the west coastal part of the country adjacent to the sea separating it from east Africa. In samples from these governorates (Haja, Al-Hodeidah and Taiz) the beta-S gene frequency probably ranges from 0.019 to 0.050 and is 0.035 to 0.044 for these regions combined. This is lower (P<0.01, \( \chi^2 \) test) than the 0.077 frequency recorded in southwest Saudi Arabia, the geographic extension of the west coastal strip of Yemen (12). A similar magnitude of difference was observed between samples from the highest frequency localities and those from their eastern neighbours including Sanaa city. The southern governorates such as Abyan, show a beta-S gene frequency of zero to 0.039 and no beta-S was detected amongst samples from the eastern and southern (desert) parts of the country such as Mareb, Al-Jawf, Shabwah, Hadramount, Al-Mahrah, Aden, Laheg and Al-Daleh. However, the number of samples collected was often too small for any firm conclusion to be drawn.

The absence of any homozygous beta-S samples in this study is probably due to a low number of samples from the west coastal governorates (Haja, Taiz and Al-Hodeidah) comprising only 15.2% of the total (228/1500). Our study shows that from these regions the prevalence of sickle cell trait is likely to be 7.0 to 8.8%, and would predict a homozygous birth rate of approximately 1 in 520 to 1 in 820, or somewhat higher, depending upon the proportion of consanguineous marriage, and easily missed in a sample size of 228. A larger sample size is needed to determine the sickle cell trait prevalence more precisely. Nevertheless, from these findings sickle cell anaemia is expected to be a particular problem in the western part of Yemen, and to which
health resources and health education for families affected could be directed. Furthermore, the lower frequency of the G-gamma globin gene-158(C-T) polymorphism amongst those who have inherited the beta-S gene compared with those who have not, indicated that the beta-S gene haplotype is not that associated with a milder course found in east Saudi Arabia.

Our study has demonstrated the first recorded case of Hb G Coushatta [beta 22(B4) Glu – Ala] in the Yemeni population. Haemoglobin G-Coushatta is not of clinical importance but other Hb variants and thalassemias may be and it would be important therefore be important to study their prevalence in Yemen.

The presence of thalassaemia genes has not been investigated in this study but PCR amplification of the DNA on the Guthrie card was shown to be good method, so it should be possible to extend this approach to study the presence of particular types of β and α thalassaemias. In those areas where double heterozygosities for β thalassaemia and beta-S occur, the rate of births affected by sickle cell disorders will be higher than that predicted from the frequency of beta-S alone. Despite careful supervision and communication regarding the manner in which the cord blood should be collected, maternal blood was present in a small number of samples. Neonatal blood collection would avoid this problem but would be much more difficult to organise.

This pilot study suggests a beta-S gene frequency amongst babies born in the capital city of Yemen that is double that obtained previously on migrants from the Yemen (5). In addition, it goes further by demonstrating an uneven distribution of the beta-S gene amongst people from different governorates. This finding is important because it raises the possibility that services can be targeted at those most in need, thus saving valuable resources. The communities most at risk in Taiz, Al-Hodeidah and Haja are not those who reside near hospitals and would therefore benefit from the development of community health services. An obvious limitation of the pilot study is bias resulting from selection of individuals from various governorates who have chosen to live in Sana’a city. The necessitating conducting subsequent studies in the localities themselves, especially in south and eastern governorates from which migration is more recent after Yemen unification.

CONCLUSION:-

The results of this study suggest an overall beta-S gene frequency of 0.011 with a higher frequency in the western coastal part of Yemen than in the central mountainous and eastern desert areas. The incidence of affected
homozygous births may reach 20/10,000 in certain areas although it is much lower than this overall. Limited health resources can best be invested in developing a program of education, screening and health care prioritising those communities residing in the western areas of Yemen with the highest beta-S gene frequency.

ACKNOWLEDGEMENTS:

The authors are grateful to Dr D. Bradley, UHW Cardiff for providing the Guthrie cards. Thanks are also due to the Leigh Douglas Memorial Fund and South Wales Glamorgan haematology Fund for help in funding this research.

REFERENCES:


**Review article: Epidemiology and Control of Viral Hepatitis " B " & " C "**

**Author:** - Dr. Ahmed M. Al-Haddad*

* Department of Community medicine. Sana'a University.
E-mail: drhadda51@maktoob.com.

Viral hepatitis is an inflammation of the liver parenchymal hepatocytes due to viral infection which mainly caused by viruses A, B, C, D, and E.

Viral hepatitis may be present without any clinical sings or symptoms (asymptomatic), with non – specific symptoms without jaundice (anicteric) or with symptoms that occur with jaundice (icteric).

Hepatitis due to other viruses viruses account for only 1 – 2 % of cases (Cytomegalovirus, Epstein – Barr virus, Herpes simplex virus, Yellow fever virus, Non A Non B Non C viral hepatitis etc).

**Fulminant Hepatitis or Acute liver failure:**

In its mots severe form acute viral hepatitis leads to extensive necrosis of the liver and may present with ACUTE or FULMINANT liver failure.

It is may also occur in some patients with longstanding viral carriage.

Tab.1. Aetiology of Fulminant Hepatitis (%)

<table>
<thead>
<tr>
<th>C-ry</th>
<th>HBV</th>
<th>HAV</th>
<th>PA</th>
<th>T / D</th>
<th>S / N</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>USA</td>
<td>15</td>
<td>8</td>
<td>18</td>
<td>15</td>
<td>39</td>
<td>5</td>
</tr>
<tr>
<td>UK</td>
<td>9</td>
<td>5</td>
<td>56</td>
<td>7</td>
<td>18</td>
<td>5</td>
</tr>
<tr>
<td>F-ce</td>
<td>46</td>
<td>4</td>
<td>2</td>
<td>20</td>
<td>19</td>
<td>9</td>
</tr>
<tr>
<td>Total</td>
<td>70</td>
<td>17</td>
<td>76</td>
<td>42</td>
<td>76</td>
<td>19</td>
</tr>
</tbody>
</table>

C-ry - Country
F-ce - France

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Clinical form of viral hepatitis:

Clinical form can be divided into states which appear as follow:-

1) Carrier state.
2) Asymptomatic infection.
3) Acute hepatitis.
4) Chronic hepatitis.
5) Fulminant hepatitis.

Mode of Transmission:

1) Blood mode Transmission (parenteral).
2) Sexual mode transmission.
3) Contact mode transmission.
4) Prenatal mode transmission.
5) Unknown.

Phases of acute state:

1) Incubation phase (period).
2) Asymptomatic periicteric phase (prodromal).
3) Icteric phase.
4) Convalescent phase.

Classification of chronic hepatitis:

Chronic hepatitis is defined as a status of vary symptoms from asymptomatic carrier phase to active hepatitis beyond 6 month and more.

It is divided to:

1) Chronic persistent hepatitis :-
   Inflammation just between the portal areas without destroying parenchyma architecture.The clinical manifestation is MILD with HbsAg.
2) Chronic active hepatitis :-

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Inflammatory activity and necrosis scattered throughout the lobular and cells of the liver (abnormal parenchyma architecture).

The clinical manifestation is SEVER with HBV – DNA, HbsAg, HbeAg, and anti HBc In “HBV ”. But anti – HCV and HC – RNA when “HCV”.

Simple Diagnostic Algorithm of viral hepatitis (How to diagnoses?).

The simple serological diagnostic test of viral hepatitis to know the causative agent should undergo 4 serological tests:-

1) HbsAg.
2) Anti – HBc (IgMAnti – HBV).
3) Anti – HAV (IgM anti – HAV).
4) Anti – HCV.

Tab. 2. Simple algorithm of serological diagnostic of viral hepatitis

<table>
<thead>
<tr>
<th>Interpretation</th>
<th>HbsAg</th>
<th>IgM Anti – HA</th>
<th>IgM Anti – HBC</th>
<th>Anti - HCV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute HB</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Chronic HB</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Acute HA on</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Chronic HB</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute HA &amp; B</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Acute HA</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Acute HA &amp; B</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Acute HB</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Acute HC</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
</tbody>
</table>

Hepatitis “B” Virus :-

Hepatitis “B” virus is a common world – wide problem characterized by an inflammatory process of liver cells in acute form which can be develop to chronic case, cirrhoses and hepatocellular carcinoma.

Virology :-

The virus of hepatitis “B” is a member a member of Hepadana – viridae contain several antigens which can infected person and make immune
response. The genome of HBV is comprises a capsule and a core containing DNA and Polymerase enzyme. The antigens of virus and their antibodies circulate in the blood where it can be very important in identifying “HBV” infection.

Genotypes of HBV :-

Genetic classification of HBV has defined six genotypes A, B, C, D, E and F. B – and C – is predominant in the Far East. F – is predominant in Americas. E – is predominant in Sub – Saharan Africa. A – and D – are more widely distributed. Also hepatitis “B” is classified into four major Subtypes (adw, ayw, adr, and, ayr).

Epidemiology of viral hepatitis “B”:-

1) Viral hepatitis “B” is a common worldwide major health problem affecting 2 billions populations (exposure).
2) The infection is endemic in most regions of the world with prevalence (carriers) of more than 300 million or about 5 % of the world population.
3) Viral hepatitis “B” may occurs in 60 – 65 % without symptoms.
4) There are three levels of “ HBV ” prevalence in the world :-

1. Highest rates :-

The prevalence of hepatitis “B” carriers (HbsAg) is 10 % and more and anti – HBs is 80 % and more.

(South East Asia, China, Equatorial Africa, Oceanic and South America).

2. Intermediate rates :-

The prevalence of hepatitis “B” carriers (HbsAg) is 5 % and more and anti – HBs is 40 % and more.

(Eastern Europe, around the Mediterranean, South America and some of the Middle East Countries).

3. Lowest rates :-
The prevalence of hepatitis “B” carriers (HbsAg) is 0.1 – 0.5 % and more and anti – HBV is 5 % and more.

(Western Europe, North America and Australia).

Viral Hepatitis “ B ” in Yemen :-

Viral hepatitis “ B ” is one of the priority health problem where it represent one of the ten common endemic diseases that play a significant role in morbidity and mortality.

The prevalence of HB carriers (HbsAg) is between 12 % and 20% some markers were found in 45.5 % of study subjects.

The carrier rate of HbsAg similar in all countries of the middle east.

HEPATITIS“B” CARRIERS:-

- Neonatal------------------90 %
- 1 Year---------------------80 %
- 5 Years-------------------10-30 %
- 12 Years------------------10 %
- Teenager and adult--------0.3-0.9 %

Prognosis:-

90 % Acute Form-Complete Recovery and Immunity from Re-infection.

10 % Chronic and Carrier state 20 % of them progress to cirrhosis or hepatocellular carcinoma (HCC) resulting in 1-2 million deaths each year.

0.1-1.1 % Fulminate---- with liver failure and death.

HEPATITIS “B” MARKERS :-

Antigens :-

1) Surface Antigen (HbsAg).
It is detectable from the first month of infection in the incubation period.

2) e- Antigen (HbeAg).
   It is a water soluble form from the protein of core antigen.
   It is detectable from the first half of the second month of infection (incubation period).
   It is indicate about the virus replicating and associated with present of HBV-DNA.
   It present beyond 6 month suggest chronic hepatitis

3) HBV-DNA Genome.
   It is detectable in serum from the first month until chronic stage.

4) Core Antigen (HbcAg).
   It is not found in the blood.

**Anti-Bodies Response:**

1) Surface anti-body or anti-HBS (anti-HbsAg).
   It is detectable from the six month after disappearance HbsAg
   and remains for life.
   It is response to:-
   
   A) Successful Vaccination
   B) Pervious HB infection (not found in carriers).
   C) Some times may be detectable in chronic infection simultaneously
   both Anti-HBS and HbsAg.

2) "e"- Antibody or Anti-Hbe (Anti-HbeAg).
   It is detectable from fourth month and remains for life.
   It is indicating that the virus "B" stops replicating in the liver.

3) Anti-HBC or (Anti-HbcAg).

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It is detectable from the first month of infection after the appearance of HbsAg and remains through the diseases stage and after recovery.

It is response to:-

a) Carrier at birth.
b) Has been infected by the virus "B".
c) Currently infected by the virus "B".

It Persists even after anti-HBS not detectable, and its persist means that there is no need for Vaccination.

4) IgM Anti- HBC.

It is a routine test used to confirm the diagnosis of acute HBV infection. IgM or Anti-HBC is important when patients with acute liver failure due to HBV and may be not present HbsAg. So in this case the IgM anti- HBC may be the only one marker can detect about the HBV infection. Levels of IgM anti-HBC may rise in patients treated with anti viral such as INTERFERON or in those undergoing spontaneous seroconversion.

**HEPATITIS “B” VACCINE:-**

Natures of vaccine are:-

1) Recombinant HB vaccine :-

   It is produced by common Backer's Yeast in with plasma containing the gene for HbsAg protein.
   or it is a vaccine which produced by DNA technology contain the gene for HbsAg.
   It is a very effective and protective.

2) Plasma derived HB Vaccine
It is an inactivated HbsAg protein purified from human plasma.

Duration of action: -

3-5 years, so there is need for BOSTER dose after five years.

Specific Treatment :-

1) Interferon
   a) Interferon alpha, beta, gamma.
   b) Peglyted Interferon alfa 2a & 2b.

2) Nucleoside analogue
   a) Ribavirin (virazol 200mg).
   b) Epivir (lamivudine 100mg, filmatalen).

3) Surgery intervention
   a) Resection.
   b) Transplantation.

Mechanism of action of interferon:-

1) Anti-proliferative effect (anti proliferation, anti-multiplication of cells)
2) Anti-viral effect (inhibits viral DNA polymerize)
3) Immune-modulator effect (stimulation)
4) More effective in “CAH” patients with high aminotransferase.
5) Unsuccessful for those who are acquired infection from the birth (HbsAg carriers at birth).
6) Unsuccessful for those who is HIV positive?
7) Unsuccessful for those who are Immune-deficient.

Interferon is administered by subcutaneous injection three time or once (pegylated) weekly in combination with ribavirin

Indication:-
1) HBV carriers with detectable serum HbsAg, HbeAg, DNA virus and elevated liver enzymes.
2) Liver fibrosis and cirrhosis (well compensated).

**Side – Effect:-**

1) Flu-like syndrome(fever, fatigue, nausea, cough and sinusitis)
2) Lethargy
3) Insomnia
4) Diarrhea
5) Depressive symptom
6) Thyroid disorders
7) Hematological disorders and hemolytic anemia
8) Impotence
9) Rheumatoid arthritis
10) Skin disorders(psoriasis, vitiligo, lichen
11) planus, itching and skin rash
12) Cardiovascular disorders
13) Psychosis and irritability.
14) Seizures
15) Peripheral neuropathy

**Contraindication:-**

**To Interferon:-**

1) Sever cardiac disease
2) Renal failure
3) Decompensated liver disease
4) Epilepsy
5) Severe neurological impairment
6) Uncontrolled thyroid disease
7) Severe psychiatric disease particularly Depression

**To Ribavirin:-**

1) severe cardiac disease
2) Renal failure
3) Decompensated liver disease
4) Pregnancy
5) Breast feeding
6) Haemoglobinopathies

**Problem of treatment:**

1) Remain expensive.
2) Have toxic side effect.
3) Low patient responding.
4) Remain the risk of relapse.
5) Rarely total elimination of the virus.

**Signs of Responding:**

1) Low HBV-DNA during the second or third month of therapy.
2) High baseline ALT during the second or third month of therapy.
3) Fall the level of HbeAg while the level of Anti-Hbe Rise
4) Rise the level of IgM Anti-HBc.
5) At the end of the course of treatment HBV -DNA should be Negative and liver enzymes are nearing Normal.

**End-Point:**

Loss of HbeAg and development of Anti-HBe, this events mark the end of viral replication, even the HbsAg remain continue it will cease in time.

**Hepatitis “C”:**

Hepatitis “C” virus infection is a common worldwide problem that may progress to cirrhosis with the subsequent development of complication such as ascetic, encephalopathy, and variceal bleeding and hepatocellular carcinoma.

**Epidemiology:**

1) Hepatitis “C” virus infection is a common worldwide problem affecting 170 million population or about 3% (carriers).
2) Hepatitis “C” virus infection is endemic in most regions of the world with the prevalence of HCV in Africa 5.3%, in Americas 1.7%, in Eastern-Mediterranean 4.6%, in Europe 1.03, in South-East Asia 2.15% and in Pacific 3.9%.

3) The prevalence of HCV in Yemen about 2-6% while approximately 5% in Saudi Arabia and 1.8% in the USA those also who are at risk of developing liver cirrhosis and or liver cancer.

4) Hepatitis “C” virus infection primarily transmitted by percutaneous exposure (65% intravenous drug use, 15% blood transfusion).

5) Vertical transmission approximately 3-7% of infant 50% of them eradicates HCV infection.

Virology:-

1) Hepatitis “C” virus is an RNA virus and a member of the flaviviride family.

2) The RNA viruses have high mutation rates.

3) The RNA viruses have different Genotypes, There are 6 known Genotypes as follow:-
   a) Genotype 1 is about 75% -common in America.
   b) Genotype 2 is about 10% - common in Europe.
   c) Genotype 3 is about 10% - common in Europe.
   d) Genotype 4 – common in Central Africa and Middle East.
   e) Genotype 5 - common in South Africa
   f) Genotype 6 – common in Hong Kong and Vietnam .

4) There is little difference in mode of transmission among the different genotypes, but there is a large difference in response to interferon medication.

Diagnostic Testing:-

1) Anti-body to multiple HCV antigens (HCV enzyme immunoassay).

2) Hepatitis C virus RNA by polymerize chain reaction.

3) Liver biopsy (to confirm HCV-RNA and to detect the severity of the disease especially fibrosis, cirrhosis and hepatocellular carcinoma).

4) Genotypes testing

Natural History:-
The majority of hepatitis “C” virus cases are asymptomatic.

2) Nonspecific symptoms such as fatigue, vague right upper quadrant discomfort and pruritus may be noted.

3) Not all patients progress to cirrhosis in fact approximately 25% progress to fibrosis and cirrhosis and 1 – 4% of them develop hepatocellular carcinoma (Hepatoma).

4) The other 75% have varying degree of chronic hepatic inflammation.

5) The average duration of hepatitis “C” infection before the onset of cirrhosis 20-50 years.

6) Factor that contribute to the development of cirrhosis are unclear but thought following :-
   a) Genetic factor
   b) Alcohol consumption
   c) Obesity

7) Neither aminotransferase elevation nor viral load correlates the inflammatory activity or the present of fibrosis in fact, but the only one way to assess disease severity is the LIVER BIOPSY.

8) The surgical therapy (resection or liver Transplantation) of hepatocellular carcinoma offers the only hope for cure.

9) The others screening like using ultrasound, Magnetic resonance imaging with gadolinium, triphasic computed tomography scan is prudent.

Specific Medical therapy:-

Interferon:-

1) Peglytaed interferon alfa 2a 180 mg per week, subcutaneous injection.
2) Peglytaed interferon alfa 2b 1,5mg/kg per week, subcutaneous injection.

Ribavirin:-

It is administered orally in divided dose by weight for Genotype I and 4 (1000 mg / day if < 75 kg and 1200mg/day if > 75kg) whereas for Genotype 2 and 3 only 800mg /day regardless of weight, ribavirin must given in combination with interferon.

Epivir (lamivudine):-

Orally 100mg per/day for at least one year.
Course of therapy:-

For Genotype 1 and 4 must receive a 48 week course but for Genotype 2 and 3 must receive only a 24 course of medical therapy.

Sustained Response Rate:-

42 - 46 % for Genotype 1 and 4.  
78 - 82 % for Genotype 1 and 2.  
54 - 56 % average.

The Decision of initial treatment:-

Must be taking into account an individual base as follow:-

1) Patient motivation.  
2) Severity of disease.  
3) Likelihood of attaining a response.  
4) Contraindication to therapy.

Indication for initial treatment:-

1) Patient with Fibrosis or Cirrhosis identified by liver biopsy.  
2) Patient with Genotypes.  
3) Patient with flu-like symptoms.  
4) Patient with extrahepatic manifestation.  
5) Patient with no contraindiction.

Note:-

It is unclear yet if therapy is necessary for asymptomatic patients with Genotype 1 and no hepatic fibroses.
Adverse Effects of specific therapy:-

**Interferon:-**

Fatigue, headache, fever and chills, nausea, weight loss, alopecia, irritability, depression, injection site reaction, autoimmune disease exacerbation (eczema, psoriasis, thyroid disease, hypothyroid and hyperthyroid, others), neutropenia thrombocytopenia.

**Ribavirin:-**

Cough shortness of breath, rash, nausea, weight loss, hemolytic anemia and teratogenicity.

**Contraindication:-**

Interferon and ribavirin are contraindicated in patients with decompensated liver disease, pregnancy, and active autoimmune disease, sever psychiatric disease, depression, hemolytic anemia, uncontrolled medical disease, poorly controlled diabetic mellitus, seizures, coronary artery disease, chronic obstructive pulmonary disease, heart failure, renal insufficiency and is teratogenic.

**Early Stopping treatment:-**

Patients who will not respond to therapy within 12 weeks of therapy by declining quantitatively HCV RNA titers more than 2 logs medical therapy should be discontinued in all genotypes of hepatitis.

If HCV RNA is detectable at week 24 for genotype 1 medical therapy should be discontinued.

**References:-**

ABSTRACT:-

Khat chewing has a degree of CNS stimulation, psychological and physiological changes; due to effects of cathinone (s-aminopropiophenone) substance which is one of the important compounds of khat. That is responsible for khat’s psychostimulant effects similar to those of amphetamine such as high mood, euphoria, alertness, hypertalkativeness, insomnia and anorexia.

An other aspect of khat is a syndrome of CNS depression, particularly after chewing such as fatigue, exhaustion, feelings of guilt, self-blame, brooding over past, helplessness and hopelessness associated with low mood, inappropiate behaviours such agitation and aggressivness The masked depressive symptoms induced by khat chewing are similar to minor depression and more near to dysthymic disorder.

KEYWORDS: khat, Catha edulis, cathinone, depression.

INTRODUCTION:-

Khat was known primarily in East Africa and spread to Yemen 700 years ago. Khat is a cultural phenomenon in Yemen. Khat has a social role in celebrations, meetings, marriages and festivities.

Khat is a common legal substance in Yemen, and its euphoric effects have been known for many centuries in East of Africa and Yemen. Because it is easily available, legal, variable in price (depends on quality) and psychological effects as euphoria, elation, improvement in sociality and
promote communication during khat consumption. These factors play an important role in its spreading in Yemen.

Khat, from catha edulis contains many substances; the most importants are Cathine and Cathinone. Cathinone has the same basic configuration as amphetamine (Schorno and Steinegger 1979) and is responsible for the psychostimulant effects. Cathinone was isolated from fresh khat ( Braenden 1979 ; Szendrei 1980 ) . Cathinone is found in higher concentration in fresh leaves ( Kalix 1987 ) , and this is why chewers prefer the fresh plant ( khat ) , that is harvested in early morning, because its potency decrease after 48h and it is transformed into cathine ( less effect) and norephedrine (Nancini et al 1989 ).

In 1985, WHO Expert Comitee on Drug Dependence recommended placing cathanone and cathine in Schedule I and Schedule II respectively.

The khat chewing is reported to cause pharmacological effects such as tachycardia, elevated blood pressure, extrasystoles, bradycardia, transient facial and conjunctival congestion, hyperthermia, mydriasis, increased respiration, increased diuresis, inhibition of micturation (depends on the fluid together intake with khat) spermatorrhea (Halbach 1972, WHO 1980, Kalix 1987, Kennedy 1987.) Other physical damages such gastritis, stomatites, oesophagitis, constipation (Halbach 1972, Luqman and Danowski 1976, Elmi 1983), insomnia is the common dominant problem, anorexia, sexual disturbance such as increased libido with good performance, decreased libido, mild erection, and rapid ejaculation (Halbach 1979, Nabil 2000).

Khat and psychosis were reported by some authors (Giannini and Castellani 1982, Gough and Cookson 1984, Pantelis et al 1989, Yousef et al 1995). I have discussed this issue in detail (Nabil 2000).

Here I will limit this discussion to khat and depression.

**KHAT-INDUCED DEPRESSION**:-

WHO 1980 in its Review of the pharmacology of khat reported insomnia and reactive depression. Kennedy ( 1987 ) reported the mildly depressive feeling with lack of energy and experienced powerless that are psychological conditioning. Abandoning the habit, however, followed by depression and the severity of depression varies and may lead to agitation and sometimes sleep disturbance (Luqman 1976).
If a random of people is asked why they chew khat, they will give very variable answers:

- to relieve boredom
- to relieve tension
- to relieve fatigue
- to relieve internal conflict
- to have a good sex
- social custom
- to spend time in fan / laugh
- to solve personal and others problems
- to study
- to protect against depression and anxiety
- to relieve the unpleasant sensation
- to increase energy
- to ease one’s mind

Others explain their chewing in an other way, to face the strain or stress that is brought by unhappy family life, marriage, low income and bad economic situation.

Others also explain that khat helps them to increase an attention and performance task.

These are the variable answers that you can get before and during khat consumption.

In those people who believe that the unpleasant feelings such as anxiety and depression will be relieved by khat chewing, the reverse is often the case, i.e khat exacerbates both anxiety and depression and they may find their depression and anxiety getting worse after chewing, and mistakenly chew more in an effort to face or cope with these feelings, and end in vicious circle. They become aware after khat, their chewing is causing harm. The awareness is associated with feelings of guilt, despair, self-blame and the chewer asks himself: Why I chew? What is the benefit? I spent all money for few moments, all problems were easy during khat, now are so difficult to manage... What I do now? I neglect my responsibility towards my family... so many questions in his mind., no answers, accompanied with severe distress and intense. They are
boredom and crying. These manifestations also exacerbate when insomnia(early insomnia) occurred which is the common sleep problem also, associated with low mood, fatigue, psychomotor retardation, loss of appetite and energy.

Many chewers after khat may experience: lack of confidence, lack of motivation, low self-esteem, inactivity, impaired skill, fatigue, exhaustion, little sleep and disturbed appetite. Others pronounced themselves well, but emphasize somatic complaints as bodily aches, pain rather than explain sentiment of boredom, sadness, despair or frustration. For example: those chewers who complain from early insomnia, fatigue, exhaustion, psychomotor retardation or agitation, push themselves to work without being well, particularly on the next morning, that associated with nervous. They explain their suffering by general weakness, bone ache, backache and headache, while others—may present their complaint of headache by own Yemeni words such as lahib berasi — heat in my head — or harig or nar berasi — burning in my head and the more interesting when they explain their pain or exhaustion (somatic) by being bewitched. You may try to discuss this issue with them, that they are suffering from long and chronic somatic and depressive symptoms and khat craving to reduce or relieve the masked symptoms of depression by the pleasant feelings resulting from khat chewing, and they try to cope these masked symptoms of depression during khat consumption only, then these symptoms are pronounced, worsed and exacerbated after khat chewing.

They refuse and do not accept the idea, that the somatic and depressive symptoms that they are suffering are induced by khat consumption. And refuse to stop or decrease khat chewing. But they are asking some vitamins to improve their health and tablets to help them to sleep.

So, these manifestations that occurred after khat are near to, or resemble in some individuals, to the symptoms and signs of minor depression and dysthymic disorder, by its chronicity but less severe from major depression symptoms.

But in some cases, that induces and exacerbates these symptoms to major depression (unipolar depression), when more frustration, becoming bad family life, bad finance issues (low-income) no family or social support, unemployed workers, and sever isolation. These act as predisposed factors and may end with major depression.
While those who originally suffer from major depression, they use and crave khat to depress or to relieve unpleasant feeling of depression, and also they believe that khat will relieve their suffering, but these feelings of guilt, low self-esteem, pessimism, despair and helplessness are exacerbated and produce an other conflict to their suffering of depression. On other hand khat also induces irritability, tension and worrying about minor events. All these behaviours do as an impulsive factor, in addition to psychological effect of khat as euphoria, they chew that, inspite of they know and aware chewing is causing harm also. So they try to cope all, by chewing more where they end in a vicious circle.

Others are depressed who craved pleasure effects to lift their spirits and to wash away sadness, boredom, and pessimism, even if only for few moments (Nabil 2000). Also these feelings are more disturbed and worsed, when insomnia and tearsdrop from the severe distress, after khat, that is associated with low mood which may induce the black ideas such as suicide. It is well known to these who are depressed, difficult to control or stop khat... In those people who are depressed, heavy and chronic chewers (predisposed individuals) khat may exacerbates psychotic symptoms as persecutory delusion even during khat chewing.

Symptoms and signs of depression are induced by khat (after khat consumption) resemble to those symptoms and signs of minor depression and more near to dysthynlic disorder.

These people who are khat chewing they describe themselves:
- by fatigue and exhaustion during a day
- loss of interest
- little sleep (early insomnia)
- inadequacy and low self-estem
- hopelessness, helplessness and hard making decisions
- brooding over past
- sensitivity to minor matters
- withdrawn
- headache, backache and muscular pain
- sexual function disturbance
- guilt and self-blame

Consequences of heavy and chronic chewing of khat to depressed individuals
- divert their income upon khat and neglect their families

-67-
interference with family and social development
family and marital disharmony and instability
family financial stress
abnormal behaviours: aggression, violence, agitation, retardation
increased risk of other substance, alcohol, drugs, etc.
increased risk of psychotic symptoms
increased cost of treatment
poor health condition
slow and less cure
poor prognosis for originally depressed individuals

Those who stop khat and are aware about the sequences of khat and its bad impact
improved in family and social relationship
stable family
decreased family financial stress
decreased cost of treatment
stop or decreased the treatment dose (those who suffer from major depression decrease the dose)
rapid recovery
improved general health condition

CONCLUSION:

Chewers especially those with low income and the unemployed think that khat certainly contributes to improvement, by believing that khat as medicine can wash away the masked symptoms and signs of depression through its euphoric feeling during khat chewing even for few moments, but the reverse is true, khat certainly contributes to improvement.

The somatic and the depressive symptoms that emphasize by chewers, interpreted to mask depression, but unfortunately the majority of chewers refuse to accept the idea about them-self that they suffer from depression. But some may become aware when they cease khat chewing, their depressive symptoms are rapidly resolved, particularly sleep and appetite improved. From this point it is simply to conclude that khat-induced depression.

One important point, those chewers who suffer from features of minor depression or dysthymia, the symptoms are also relieved or diminished, when chewers stop khat.
While, others who cope the unpleasant feelings by excessive chewing, they come to an end of vicious circle, by worsen the depressive symptoms, and may exacerbate to major depression (unipolar). On the other hand the bad sequences of that include the family instability, neglect the needs of family, finance stress, daily quarrels may lead to family unit breakdown. In addition to lost time, productivity, also abnormal behaviours — aggressiveness, violence arise especially among those people who are unemployed workers to get money to buy khat.

As reported by WHOM Expert Commitee (1985) khat has a degree of CNS stimulation, an other aspect of khat has a degree of CNS depression, (post khat-depression) also.

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ABSTRACT
Neurotic disorders among qat chewers and non-qat chewers in Yemen.

Author:- Mohammad Ali Noman, 1998
Tel.: 73892933

ABSTRACT:-

The aim of this research is to find out neurotic disorders among two groups: an experimental group, whose individuals used to chew qat, and a control group, whose individual never tasted it.

In order to achieve the purpose just above, the following questions were raised:

1. Are there any significant differences in neurotic disorders among people who are addicted to chewing qat in such as: anxiety, phobias, hysteria, depression and obsession?

2. Are there any significant differences among qat chewing individuals according to time duration?

3. What are the most neurotic disorders found out among qat chewing people?

The sample situated was drowning out from Sana’a population (manipulity). A Number of the sample was (300) male, were divided as follows:

1st:- experimental group of (200) individuals:

- 100 persons used to chew qat for (5) hours a day, throughout (5) years.
- 100 persons chewed qat for (10) hours a day, throughout (5) years too.

2nd:- control group, whose individuals never chewed qat at all. no.of individuals (100).
To find out neurotic disorders among those who used to chew qat and in order to compare their cases with the control group, the following psychiatric nervous scale was amplified:

(anxiety-phobias-hysteria-depression-obsession) the scale was prepared by Dr. Abdul-rahman Issawi. No of the items (124).

The scale was adapted to suit the Yemeni environment validity of the scale was manipulated by means of jury judgment.

Division was made that any item might by less than 78% should be eliminated. Accordingly, (2) items have removed from the scale, because they got only 66% the investigator recover to discriminative validation to value the items of the scale.

Hence all items appeared to be valid, except the two items which were dismissed as just mentioned above. So by that the shape of the scale becomes consisted of (122) items.

Reliability was tested as follows:

(40) Persons were taken to apply the inventory upon them.

Pearson is correlation-coefficient was used for this purpose.

It finds that the correlation-coefficient was 96%. Applying the inventory to the investigated sample, the investigator got the following points:

1. There have been significant differences among those who used to chew qat, distinguishing them from those who did not chew it. Various neuroses appeared among them except the depressions.

2. It was found out that there are significant differences among the investigated groups, according to time duration, the longer they chewed, the more neurotic disorders they suffered.

3. The final results have also shown that the neurotic anxiety and the neurotic depression, have been the highly correlated with chewing qat. Therefore, there is a strong relationship between chewing qat addiction and neurotic disorders.
Economics of health in the Republic of Yemen
“A theoretical and practical study”

Authors: Gamal Saeed Mohamed Ali El-Zaemey
Faculty of commerce — al Hodidah University,
E-mail: alzaeemi@hotmail.com, Tel: 04 253909
Ph.D. Thesis in Economics of health.

Abstract:

The aims of this study are to identify the Efficiency of allocating government spending which is necessary for improving the health status of the population and enhancing the economic growth in Yemen.

The methods:

- Statistical analysis for estimating the function of health production in Yemen, aiming at identifying the most efficient factors in improving the population health status in Yemen.

- Statistical analysis was also used to estimate the Schultz-Dennison growth model in order to calculate the return from investment in human capital for the purpose of identify the most efficient factors in speeding up economic growth in Yemen.

- Economical evaluation methods such as Cost-Effectiveness Analysis, Cost - Benefit Analysis for investment of Immunization programme in Yemen and the estimation of the magnitude of the economic burden of infectious diseases in Yemen (2001) were used for the purposes of identifying the fact that investment in health especially in programs of infectious diseases control is a main determinant in the performance of the national economy.
The conclusions:

- The economic and environmental factors are the main determinants of the health productions efficiency (improving the population health status) and are of more influence than health services. The priorities of government spending necessary to achieve the highest health production with the least-cost are: the increase per capita of consumption of pure water, followed by increasing spending on health services, reducing birth rates, increasing employment and increasing the number of students, respectively.

- The investment in health is a main determinant of the efficiency of national economy; this is evident through the following results:

  - The average contribution of health in the economic growth is (23.4%) and the average for education contribution is (35.4%) which is greater than the contribution of material capital (8.8%) throughout the period from 1978-2001, this means that investment in health has a higher efficiency than material investment in speeding up economic growth in Yemen.

  - Investment in health - especially in expanded immunization programs and programs of infectious diseases control and treatment - will be transformed into additional return of millions of dollars annually which can be used for enhancing the economic growth in Yemen. Some results have shown that investment in expanded immunization activities is of high economic efficiency because every dollar spent on a complete immunization against the six diseases of childhood saves 145 $, and every dollar spent on immunization against hepatitis saves 75 $. In addition, the economic burden of infectious diseases is estimated at around 4.14 $ million in 2001. Which is about 42.7% of the gross national production. This means that poor health weakens the economic development and that investment in health enhances economic growth.

In the light of the previous results, the study suggests that a health care policy that is based on focusing primarily on fancying health services and ignoring economic, environmental and educational factors will be ineffective and is of little benefit in achieving the goal and improving the health status of
the population. Likewise, a developmental policy based on focusing primarily on materialistic investments and ignoring services that help in assisting the health status of the population will end in failure and is of little benefit in achieving economic growth.

Therefore, the study recommends adopting a strategy of integration between health development and economic development. Such a strategy requires the construction of a development policy that gives the priority in allocating expenses to investments that improve the health status of the population and limit the material investments.

On the other hand, the study recommend adapting a health policy based on giving the priority to allocating health expenses for the expansion in essential preventive and therapeutic health services that undertake the task of control and treatment diseases that make up the greater portion of disease burden in Yemen on the expense of complicated therapeutic care in specialized hospitals.

This requires starting to respond to the needs of the governrates on the basis of the numbers their populations and their health needs, along with focusing on the most deprived governrates which are: Al-hodeidah, Taiz, Amran, Saadah and Laheg because they carry the larger portion of disease burden in Yemen.