Original article

Screening program on hepatitis B in young Albanian population: The Greek-Albanian collaborative study on the prevention of hepatitis B (the HEPAGA project)

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SUMMARY

Aim: **The aim of the study was to screen for hepatitis B virus (HBV) in a well-defined, young, population in the area of Tirana, Albania (the HEPAGA project).**

***Patients-Method*: This study was conducted under the auspices and with grants from the Greek Ministry of Development and the Albanian Ministry of Education and science. This collaborative study lasted for two years (2001-2002) and was successfully completed on both sides. Serum samples from the non-vaccinated, young population (ages 14-20) living in a well-defined area of Tirana were collected during the period from September 2001 to February 2002 and were stored at -20° C until assayed at the Blood Bank of the Ioannina University Hospital. Every sample was examined for HBV immunology profile using routine methods. In case of gray zone results double testing was performed. In cases of insufficient serum we tested, in priority, HBsAg, then HBcore antibody (anti-) and then anti-HBs. Results were then sent back to Albania where Albanian gastroenterologists informed the population tested of their HBV status and the need for vaccination or treatment.**

Results: **The Greek part received 412 serum samples. Two samples could not be evaluated for technical reasons, while the remaining 410 were analyzed for the HBV immunology parameters as shown below.**

Parameter tested	No of samples	%
Hepatitis B virus not detected	226	54.88
HBsAg(+)	49	11.89
HBcore(+)/anti-HBs over 10 UI/ml	87	21.19
HBcore(+)/anti-HBs less than 10 UI/ml	14	3.49
Only HBcore(+)	14	3.49
HBcore(+) not enough serum for anti-HBs	8	1.97
HBsAg(-) not enough serum for HBcore	12	3.09
TOTAL	410	100.00

Conclusions: **The HEPAGA Study showed that public health projects between Balkan countries are realistic. Albania is a paradigm of public health prevention strategy directed at the elimination of hepatitis B through an expanded, obligatory vaccination programme.**

Key words: hepatitis, HBsAg, Albania, Greece, screening, population study

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INTRODUCTION

The high prevalence of viral hepatitis B in Albania still remains a serious problem of community health in the area of the Balkans. Additionally, the remarkably high numbers of patients with chronic liver disease and hepatocellular carcinoma in this area are an obvious mid-

term result of this phenomenon[1,2].

North-West Greece, which borders South Albania, has, during the last decade, received a large number of young Albanian refugees. This new immigrant population is characterized by a high incidence of infection with hepatitis A, B, C and D viruses[3-6]. This will probably increase the prevalence of infection with hepatoviruses in Northwest Greece during the next decade. Urgent vaccination and information programmes in Greece and Albania are mandatory for the prevention of an epidemic phenomenon in this region as well as for the elimination of number of patients with chronic liver diseases and hepatocellular carcinoma[7].

For this reason, a common action programme (HEPAGA) with shared responsibilities was proposed in 2000 by the Hepato-Gastroentrology Units of the University Hospitals of Ioannnina (Greece) and Tirana (Albania) with the cooperation of the Department of Internal Medicine of the General Hospital of Filiates (Greece) [Figure]. The title of this programme was "*Screening for hepatitis B in Albania: The Greek-Albanian collaborative study (HEPAGA) on the prevention of hepatitis B and hepatocellular carcinoma in Albania*".

This programme was completed in 2003 and its description and results are presented here.

Figure. The North-west Greece-Albanian region collaborating in the HEPAGA project.

STUDY PATIENTS & METHODS

HEPAGA: a Greek-Albanian collaboration study on hepatitis B screening

This project (HEPAGA) is a North-West Greece-Albania Collaborative Study on epidemiology, diagnosis, prevention and treatment of viral hepatitis B and its long-term complications including chronic liver disease and hepatocellular carcinoma. The study was accomplished using traditional (site visits) and modern methods of medical communication and information (e-mailing).

Throughout this bilateral project, it was possible for the first time in this Balkanian region to describe the real impact of hepatitis B and to further assess the prevention and treating strategies on hepatitis B, which were introduced in Albania a decade ago. Additionally, this project represented a bridge between doctors, especially the young ones, for learning, communicating and contributing to their patient's quality of care and quality of life. Finally a decrease of morbidity due to hepato-cellular carcinoma and viral hepatitis was targeted as a long-term result.

During proposal submission the goals and objectives of this bilateral, shared-action project were defined as the following:

1. Short term visits dedicated to research and training (North-West Greece-Tirana).
2. Joint workshops, joint publishing of results and presentation of results at international conferences within the two countries (Greece-Albania).
3. Installation and expansion of a Hepatitis Health Network system in this area of the Balkans where the Greek and the Albanian Hepato-Gastroenterolgy Units are the only leading health care structures.

HEPAGA routine protocol study

This study was conducted under the auspices and grants from the Greek Ministry of Development and the Albanian Ministry of Education and Science. This collaborative study lasted two years (2001-2002) and was successfully completed on both sides by the end of 2002. Serum samples from non-vaccinated young population (aged 14-20 years) living in a well defined area of Tirana were collected during the period from September 2001 to February 2002 and were stored at -20^{o} C until assayed at the Blood Bank of the Ioannina University Hospital. The young population group, which was tested, consisted of students of all classes of the "Technical School of Tourism" located in Tirana. The students' origin was from

any part of Albania while there was sample homogeneity regarding gender and age groups. The students' socio-economic status was that of the mean Albanian citizen.

Every sample was examined for HBV immunology profile using routine methods. Blood screening, when finalized, was again checked and then records were sent back to Tirana where the Albanian team informed all participants of their HBV status and, furthermore, of the need for vaccination or treatment, if necessary. In addition, information from previous screening studies for hepatitis B in Albanians coming to Northwest Greece was used as documentation source.

Blood screening for hepatitis B-serological studies

Coded sera were tested in February and March 2002. Antibodies to HBsAg (HBsAb), HBV core antigen (HBcAb) as well as hepatitis B surface antigen (HBsAg) were detected using commercially available enzyme immunoassays (IMX, Abbot Laboratories, Wiesbaden, Germany).

Every sample was examined for HBV immunology profile using the above-mentioned routine methods. In cases of gray zone results, double testing was performed. In cases of insufficient serum (inadequate quantity) the following test were performed in the priority order: HBsAg, then HBcore antibody (anti- HBcore) and then anti-HBs.

All results from serum evaluation were compared with data from the Northwest Greece population and data from previous studies with Albanian refugees in Northwest Greece and other countries.

RESULTS

The Greek part received 412 serum samples. Two samples could not be evaluated for technical reasons while the remaining 410 were analyzed for the HBV immunology parameters.

In this cohort, 226 samples (54.88%) were negative for hepatitis B virus, while 49 samples (11.89%) were HBsAg positive. Antibodies against hepatitis B in protective titles (over 10 UI/ml) were detected in 87 (21.19%) serum samples which were also HBcore(+), indicative of previous HBV exposure.

Antibodies against hepatitis B in non-protective titles (less than 10 UI/ml) were detected in 14 (3.49%) serum samples which were also HBcore(+) indicative of previous HBV exposure (Table).

Table. Results of the serum testing for hepatitis B markers in 410 Albanians aged 14-20 years (the HEPAGA study).

Parameter tested	No of samples	%
Hepatitis B virus not detected	226	54.88
HBsAg(+)	49	11.89
HBcore(+)/anti-HBs over 10 UI/ml	87	21.19
HBcore(+)/anti-HBs less than 10 UI/ml	14	3.49
Only HBcore(+)	14	3.49
HBcore(+) not enough serum for anti-HBs	8	1.97
HBsAg(-) not enough serum for Hbcore	12	3.09
TOTAL	410	100.00

In 8 samples (1.97%) with HBcore(+), testing for anti-HBs was not possible due to limited serum quantity; the same happened to 12 HBsAg(-) samples (3.09%) where serum was insufficient for HBcore testing.

DISCUSSION

This bilateral Greek-Albanian collaborative study on hepatitis B succeeded not only in providing medical information about hepatitis B prevalence in the region of Tirana, but also in strengthening medical collaboration in the Balkans. The benefits of this medical collaboration can be briefly described under the several topics that follow.

Scientific bilateral amelioration was achieved through research and training visits, as well through analytical literature review on common interest issues, such as this of hepatitis B. In addition, the basis of a Health Care Network system on hepatitis B between the two countries has been created.

Optimizing quality of care and quality of life in patients with hepatitis B still remains an important topic of public health across Europe. During this collaborative study the term of Preventive Hepatology was created and applied successfully to a young, Albanian population who underwent hepatologist consultation and hepatitis B testing without any kind of charge. Prevention of viral hepatitis (Vaccination programme) remains the main topic of interest in modern Preventive Hepatology[8-11]. Thus, all individuals needing vaccination for hepatitis B underwent vaccination (3 doses) and follow up serological testing. Treatment of viral hepatitis B was offered when needed. In fact, all HBsAg(+) individuals were informed about their health status and were offered treatment and regular follow up. All tested individuals

will be followed up in the next years in order to reassess their immunoprotection against HBV and to reveal any kind of need for further diagnostic or therapeutic intervention .

Early diagnosis of hepatocellular carcinoma, as well as prevention of viral hepatitis B derived hepatocellular carcinoma, represents another interesting topic for scientific research in areas with high hepatitis B endemicity[1,12-13]. This study took the first step towards prevention by identifying HBsAg (+) carriers and by offering vaccination to individuals lacking hepatitis B protective antibodies. However, a lot of work has yet to be done for many other patients with chronic hepatitis B with or without evidence of cirrhosis, outside this young population.

Common bilateral workshops were started in 2001 and common publications in the form of abstracts or full papers have been and are being written. Furthermore, this project resulted in optimizing medical collaboration within two areas and in new upcoming proposals for future scientific collaboration. In 2003, a new bilateral project under the auspices and with grants from the Greek Ministry of Development and the Albanian Ministry of Education and Science started (HEPAGA II project) and will hopefully be completed in 2005.

New epidemiological data on hepatitis B is always of great interest and importance in the area of the Balkans, which is considered to be an area of major public health interest because of its high young, migrant population. Regional and European policy on health care and prevention depends to a considerable extent on the epidemiological information of such studies[14,15].

This study in comparison to relevant studies in Greece[5,15,17], Albania[1,7] and Italy[3,4,6], clearly shows the decreasing prevalence of hepatitis B (HBsAg+) in Albanian population through the years. This is the result of the expanded vaccination programmes for hepatitis B in Albania, as well as of the improvement in living conditions and socioeconomic amelioration of Albania during the last decade[16].

In 1995, according to a study from our Department[5], the prevalence of hepatitis B (HBsAg+) in Albanian refugees to Northwest Greece was approximately 22% regardless of age. In addition, one year later, in 1996, a study from Athens[17] showed that the prevalence of hepatitis B (HBsAg+) in pregnant Albanians was 13.4%. In an unselected group of 130 Albanian refugees in the area of Athens (mean age 31.7 years) the prevalence of hepatitis B (HBsAg+) was 15.4%[18]. In studies of young adults from Nigeria the prevalence of hepatitis B (HBsAg+) was up to 21.3%[19-20].

Albania is a paradigm of public health prevention strategy towards elimination of hepatitis B prevalence through an expanded obligatory vaccination programme. This programme started in the early 1990's and a decade later, according to available data, has succeeded in eliminating by half the prevalence of hepatitis B (HBsAg+). If this rate continues, it seems realistic to predict that after 2010 Albania will enter the list of moderate endemicity for hepatitis B countries. Hepatocellular carcinoma, related to hepatitis B, will also, hopefully, be decreased but data are not available for such a comparison.

Refugees from southern Albania are a new immigrant population characterized, especially for its younger members, by a high incidence of markers of infection with hepatitis B virus.

Recent studies in Northwest Greece and Southern Italy provide evidence for a very high prevalence of markers of HAV, HBV and HDV infection in an unselected but well-defined population of refugees from southern Albania compared with controls of Greek and Italian nationality[3,5,7]. In Southeast Europe where HBV acute and chronic infection is a major health problem, selected risk group vaccination policy will have no impact on this infection and will not be able to further control transmission from this young carrier pool. In addition, the increasing numbers of immigrants from high or even intermediate endemicity regions contributes to hepatitis B transmission in the low endemicity countries, including Greece and Italy.

In conclusion, the Greek-Albanian Collaborative Study on Hepatitis B has shown that bilateral public health projects between Balkan countries are realistic and fruitful. Results are always interesting, as such epidemiological data on Preventive Hepatology is not commonly available. In addition, such information contributes towards European and WHO policy for preventive medicine and the elimination of epidemic diseases.

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