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Adoption of Euvax-B vaccine in Nineveh

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Hepatitis B infection is one of the most important health problems around the world. The high mortality rate of the hepatitis B encouraged research that led to the finding of an effective vaccine against it. The aim of the present study was to find out the use of the Euvax-B vaccine in sectors of Nineveh province. According to the results obtained in this study, in the next five years, the vaccination coverage for the second and third doses needs to improve.

Keywords: vaccines; hepatitis B virus; hepatitis B surface antigen; immunization; *Hepadnaviridae*.

Introduction

Hepatitis B infection is a global health problem caused by Hepatitis B virus (HBV). This virus is 50-100 times more infectious than the human immunodeficiency virus. Approximately 400 million people carry chronic liver disease each year due to the consequences of the disease.⁽¹⁾ HBV occurs as an acute or chronic, and occult infection. Some cases may develop cirrhosis and hepatocellular carcinoma.^(2,3) People at high risk of infection include those who require frequent transfusions, hemodialysis patients, and healthcare workers such as physicians, dentists, and nurses. Intravenous drug users, police, firefighters and others who come into contact with infected blood products are also exposed to the infection,⁽⁴⁾ as well as, sexual contacts of both, acute and chronically infected persons. HBV is classified under the *Orthohepadna* virus genus within the *Hepadnaviridae* family.⁽⁵⁾

HBV is a small DNA virus with a 42 nm particle.⁽⁶⁾ The relatively small genome generates different proteins, among them, polymerase, core (HBcAg), early (HBeAg), small surface-antigen (HBsAg), and the X protein. HBcAg and HBeAg are encoded from the C gene.⁽⁷⁾

The small surface protein of the hepatitis B (HBs) is coded by the S gene. This protein is the primary component of all forms of hepatitis B particles. It is produced in high quantities. It also contains a highly antigenic epitope, called HBsAg, which is

a modulation antigen on which the virus serotype classification depends. In the major hydrophilic region, the “a” determinant has an assumed two-loop structure located on the virion surface. This two-loop structure encompasses conserved residues (124-147). HBs also comprises the basic structure of the HBV vaccine.^(8,9)

Hepatitis B Vaccine

The World Health Organization (WHO) recommends the hepatitis B preventive vaccine for all newborns in severely endemic areas and at-risk groups in low endemic areas.⁽¹⁰⁾ Hepatitis B vaccines are used for active immunization. The United States (US) Food and Drug Administration (FDA) licensed the first plasma-derived vaccine in 1981. Later, the vaccine was replaced by a recombinant version, which displays HBsAg, synthetically produced by *Saccharomyces cerevisiae*. This vaccine became available after has been licensed by FDA in 1986 and it is currently documented and used in the US. Vaccine efficacy studies reported 90-100% protection and the vaccine also proved to be effective in young children and infants, even though young children are poorly responsive due to their immature immune system.^(11,12)

Currently, the second-generation of DNA-recombinant vaccine has been used since 1991. It is important to know that the recombinant vaccine works as an anticancer by preventing the formation of hepatocellular carcinoma.⁽¹³⁾ Nowadays, Recombivax

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HB (Merck) and Energex-B (GlaxoSmithKline) single antigen vaccines are used. Comvax (Merck), is a combined vaccine that contains *Haemophilus influenzae* type b conjugate antigen and the recombinant HBsAg. Three doses of Comvax should be administered at 2, 4, and 12-15 months. The Centers for Disease Control and Prevention recommends that newborns receive monovalent HBV vaccine at birth followed by three additional doses of the combined *Haemophilus influenzae* type b conjugate antigen and HBsAg vaccine. Other vaccine combination consists of recombinant HBsAg, diphtheria, tetanus, pertussis, and inactivated poliovirus. For children under 6 weeks or over 7 years old, this vaccine is not approved. Another vaccine combination includes inactivated hepatitis A and recombinant HBsAg (Twinrix, GlaxoSmithKline). This vaccine is indicated for people over 18 years who are vulnerable to the hepatitis A and HBV virus. This combined vaccine also extends to immunocompromised patients. All vaccines were subtype (*adw*) derived from HBsAg and did not appear to be significantly different.^(14,15)

Hepatitis B vaccines provide defence against both homologous and heterologous HBV subtypes presumably through anti-a antibodies. The development of monospecific anti-d response in the absence of anti-a, and subsequent HBV reinfection after hepatitis B vaccination, has been documented.⁽¹⁶⁾

In people with acute hepatitis B, the vaccine is considered insufficient. Moreover, it is not necessary for individuals positive to HBsAg or with a known previous infection (anti-HB). However, immunization should not be delayed while waiting for any test results.⁽¹⁷⁾ Vaccines for mutants in the S region (sG145R and sT126A/S) are estimated to account for almost half of infection permeations.⁽¹⁸⁾

Vaccine escape from HBsAg mutations is the primary goal of immune viral neutralization, either by normal or vaccine-induced anti-HBs antibodies. However, genetic and structural qualifications limit major protein changes. The complex secondary and tertiary structure of HBsAg has not fully understood yet, so vaccine production is still ongoing. The primary working model contains four trans-membrane helices, has many residues at the N and C terminus and a major hydrophilic region (approximately residues 103-173) exposed on the surface of viral particles. The immunodominant “a” determinant is the major target for most neutralizing antibodies, the main goal of the HBsAg detection tests.

The determinant “a” consists of loops two and three. Besides, the HBsAg signalling region encodes a portion of the reverse transcriptase enzyme of the viral DNA polymerase domain. Some of the deletion mutations announced, have been isolated from long-lived HBV vectors and may represent clogged products. Small fragments of insertion can also observe in loop one of HBsAg. They were isolated from HBsAg seronegative patients, at least when using monoclonal antibody-based assays. Although these insertions do not take place within the determinant “a” itself, they can affect its structure. Unvaccinated individuals may undergo vaccine escape mutations, as they exist as secondary viral populations. They have only emerged to become the main viral populations in patients with immune pressure. Liver transplant patients under vaccine-induced treatment or prophylaxis, usually test positive to human anti-HBs immunoglobulins.^(19,20)

HBV vaccine in Nineveh

As part of the extended immunization program in Iraq, the hepatitis B vaccine was launched in 1990. WHO is not only promoted the sight production of the HBV vaccine in Korea, but also commanded changing in hepatitis policy.⁽²¹⁾ Recently, the Euvax-B Inj. (LG co., Korea), a recombinant HBsAg vaccine, has been administered in 3 doses to adults ≥ 15 years, at all central public health in Mosul city and in all sectors of Nineveh province. There is a wide campaign to use the vaccine to reduce the proportion of mortality due to chronic HBV and serious complications resulting from HBV infection. It must achieve a 95% coverage rate for the third dose of vaccine, for children under 1 year old. Since the first week, the vaccine should be administered to children and three doses are required for safety.

The analysis of coverage data for the years 2009-2019 in Nineveh province showed that the coverage rates were very good for the first dose (for all years) and decreased slightly for the second and third doses; the discontinuity in getting the vaccine by reviewers influenced these results (Fig. 1). The relative coverage of the third vaccine dose for the years 2009-2011 was 97%, 94.3%, 94.4% respectively, but fell (82.8%) in 2012 as a result of the entry of new vaccines, some bugs in the goals to be achieved and the fact that the HBV vaccine was coincident with the Polio vaccine. Data were missed from 2013-2017 because of the war. In 2019, the ratio declined to reached only 75.8%, due to the reasons that have been mentioned (Fig. 1). The monthly

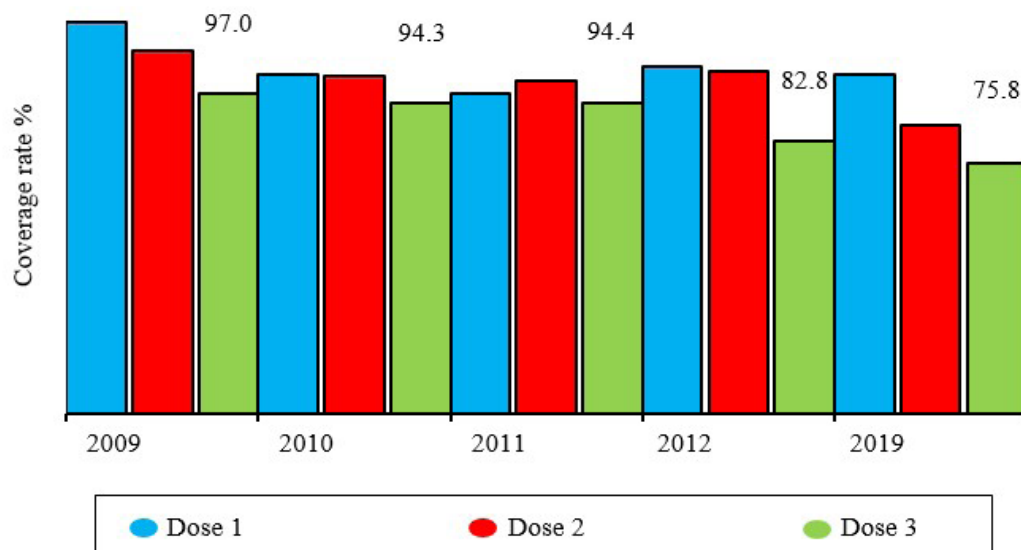


Fig. 1. Coverage rate of Euvax-B vaccine during 2009-2019 in Nineveh province, Iraq.

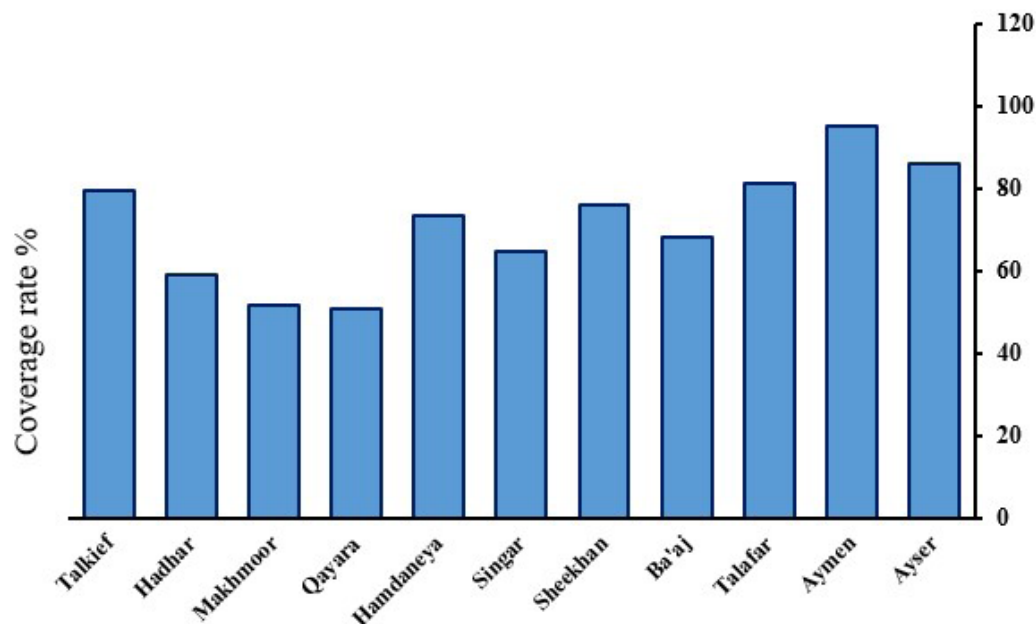


Fig. 2. Distribution of Euvax-B doses according to the sectors of Nineveh province, 2019.

coverage ratios for 2019 had little variation during this year; they plummeted with the scarcity of vaccine in October (reached only 50.1%) and then rose to 88.9% in November, with the availability of the pentavalent vaccine (DPT-Hep B-Hib), often referred to as the 5-in-1 vaccine, that protects against diphtheria, pertussis, tetanus, hepatitis B and *Haemophilus influenzae* type b.

For the vaccine distribution on sectors of Nineveh province, the percentages were much lower in the Ba'aj (68.3%), Hadhar (58.9%), Makhmor (51.5%) and Singar sectors (64.7%) as is shown in Figure 2.

In addition to the above-mentioned factors and the lack of supply of the polio and pentavalent vaccine, the migration of the population to the security situation and the difficulties of reaching health centers contributed to a decline in the number of vaccine recipients.^(22,23)

The HBV vaccine has also been given to adults working in health institutions, particularly: surgeons; dentists; nurses; service staff in birth galleries, processes and lounges, emergency, kidney washed lobbies; working staff in laboratories and blood bank centers; blood

Table 1. Number of doses of the HBV vaccine given to adults through 2018 in Mosul city.

Third vaccine dose	Second vaccine dose	First vaccine dose
9238	9259	13708

transfusion patients (specially who need frequent blood transfusions) and those who work in midwifery. The Table 1 shows the number of doses administered to the groups above in 2018.^(24,25)

Conclusion

The incidence of clinically diagnosed hepatitis has declined sharply in recent years due to the availability of laboratory tests and public awareness of the need to administer all doses of the vaccine. The gap between the amounts of the first vaccine dose compared to the third dose was relatively high in 2019, so the vaccination coverage for the second and third doses needs to improve, and this is what we expect to the future. In the next few years, we aim to reduce this variance with the effort from all sectors of society.

Conflict of interest

The authors declare that there is no conflict of interest.

Author's contributions

Ali A. Dawood designed the study, performed and wrote the first draft of the manuscript.

Mahmood A. Altobje managed the literature searches.

Zeyad T. Al-Rassam the rest of the authors read and approved the final manuscript.

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Empleo de la vacuna Euvax-B en la provincia de Nínive

Resumen

La infección por hepatitis B es uno de los más importantes problemas de salud del mundo. La alta tasa de mortalidad de la hepatitis B impulsó las investigaciones que llevaron a encontrar una vacuna eficaz contra la misma. El objetivo del presente estudio fue conocer el uso de la vacuna Euvax-B en sectores de la provincia de Nínive. De acuerdo con los resultados obtenidos, en los próximos cinco años, se debe incrementar la cobertura de inmunización de la segunda y tercera dosis de la vacuna.

Palabras clave: vacunas; virus de la hepatitis B; antígenos de superficie la hepatitis B; inmunización; *Hepadnaviridae*.

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