

False positive Hepatitis B Surface Antigen due to recent vaccination

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Abstract:

Objective:

Hepatitis B is the most common viral hepatitis, potentially life threatening, with long term complications. Currently, vaccine is the most effective tool against hepatitis B infection. It is worthwhile mentioning that due to rampant use of hepatitis B vaccine (HBV), there have been concerns about hepatitis B surface antigen (HBsAg) reactivity. This article aims to report the false positive results of HBsAg due to recent HBV among healthy male adults.

Subjects and Methods:

The subjects were selected from a Community Health Center, under the umbrella of a tertiary care hospital, Saudi Arabia. The data was retrieved from electronic medical records maintained at the clinic.

Results:

A total of 130 employees were recruited, only 117 records could be retrieved from the system. The mean age of participants was 31.34 ± 12.73 years. The administration of HBV and HBsAg test was performed simultaneously. The lab reported three cases of HBsAg positivity, a false positive result of 2.56%. Repeat testing after one week for HBsAg was negative for the three cases.

Conclusion:

This study confirmed that HBsAg reactivity might be seen in regular screening programs for healthy adults.

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Introduction:

Hepatitis B is one of the most common viral hepatitis, potentially life threatening, with long term complications like cirrhosis and hepatocellular carcinoma. It is a global health problem, transmitted through blood and body fluids and the causative organism is hepatitis B virus. According to a WHO report, around 2 billion people are infected with hepatitis B virus (HBV) in the world, and about 600,000 people die annually due to its acute or chronic consequences. There are more than 350 million HBV carriers in the world. ⁽¹⁾ Currently, vaccine is the most effective tool against hepatitis B infection accepted universally. The vaccine against hepatitis B became available in 1982, when it was given to certain special population. At present, recombinant hepatitis B vaccine is routinely given to adults and children as part of the immunization program worldwide. Center for disease control recommend three doses of hepatitis B vaccine at 0, 1 and 6 months. ⁽²⁾ The high risk population for contacting the infection is blood recipients, hemodialysis patients, infants born to mothers infected with HBV, men having sex with men and intravenous drug users. ⁽¹⁾

It is worthwhile mentioning that due to rampant use of hepatitis B vaccine, there have been concerns about false positive hepatitis B surface antigen (HBsAg) reactivity. This subject has been of interest since the 1990s, few years after the introduction of vaccine. Earliest case report was by Challapalli et al, who documented antigenemia in a neonate following hepatitis B vaccine. ⁽³⁾ Soon after, Bernstein et al showed 65% infants were tested positive, and HBsAg results tested negative for all after 18 days. ⁽⁴⁾ Few years later, Koskal et al revealed 69.2% infants showing false positive antigenemia after the vaccine, although it was transient and was cleared 28 days post vaccination. ⁽⁵⁾ A more recent paper by Fleisher et al has also observed transient antigenemia with Pediarix, a combination vaccine. ⁽⁶⁾ Another recent case report by Mantadakis E et al of an infant also documented transient antigenemia that cleared 18 days after the Infanrix Hexa, another combination vaccine. ⁽⁷⁾ During the 1990s, the

topic gained popularity among hemodialysis patients who were offered routine vaccination and screening for Hepatitis B infection. Janzen et al was the first one to report positive HBsAg among hemodialysis patients, where they turned negative within 20 days of vaccination. ⁽⁸⁾ Shortly after that, Broderson et al also reported a case of transient antigenemia in hemodialysis patient subsequent to third dose of Hep B vaccine, which cleared one week after vaccination. ⁽⁹⁾ In early 2000s, Ly D et al found nine hemodialysis patients to be HBsAg positive attributed to vaccine that was also transient. ⁽¹⁰⁾ The antibody response to the vaccine is well established, and the affect of vaccine on hepatitis B surface antigen (HBsAg) has been studied among infants and hemodialysis patients. There are reports of false positivity of HBsAg among healthy blood donors, however, scanty data could be found for adults undergoing health screening programs. This article aims to report the false positive results of HBsAg due to the recent Hepatitis B vaccine among healthy male adults.

Methods:

This is a case series where the subjects were selected from a Satellite Clinic, a Community Health Center, under the umbrella of a tertiary care hospital in Saudi Arabia. The clinic is located inside a residential compound inhabited by employees of a Petrochemical Company and their families. A regular annual screening program for certain cadre of employees was scheduled during a six month period January to June 2013. The list of the employees enrolled in the program was obtained from the Petrochemical Company Medical Representative at the Clinic. A total of 130 employees were enrolled in the program as per the company's initiative, out of which only 177 candidates reported for the examination. The employees selected for the program belong to the emergency response team for the petrochemical industry. The records were retrieved from the medical records maintained at the clinic through a computerized system. In addition, a verbal informed consent was obtained from him to use the data only for research purposes, maintaining confidentiality of the employees by keeping them anonymous. All the candidates,

who were considered generally healthy, attended the Clinic, full complete physical examination was performed, and specific lab tests were ordered. Among other tests, Hepatitis B Surface Antigen was also requested, the sample was sent to the main lab at the parent institute. The candidates received Hepatitis B vaccine as they completed the examination, Engerix B (Glaxo SmithKline Beecham Pharma) was administered intramuscularly as 1mL single dose vial in deltoid muscle at the first visit, followed by scheduled doses at 1 and 6 months. After the clinical examination was completed, blood samples were tested for HBsAg by a third generation Chemiluminescence assay using ROCHE reagents according to the manufacturer's instructions by means of machine COBASe601.

Results and Discussion:

A total of 130 employees were recruited, who attended the clinic for annual health screening and check up program, only 117 records could be retrieved from the system, therefore rest were excluded. The mean age of participants was 31.34 ± 12.73 years; all were males as it is a program for special cadre of population, the emergency response team for the petrochemical industry. During the first month of program initiation, the administration of hepatitis B vaccine and the test for HBsAg were performed simultaneously. The lab reported three cases of HBsAg positivity, and informed the clinicians, the false positive result turned out to be 2.56%. The samples tested positive, were called back again to the clinic, relevant further tests were done to exclude active Hepatitis B infection and follow up testing of HBsAg after one week turned out to be negative. After this incidental finding, the other candidates were first sent to the lab for testing and after the results obtained, were offered vaccine. None of the participants result exhibited HBsAg positive after this step taken. The present study results augmented the findings of earlier research undertaken among different cadres of population. During early 1990s, Kloster B et al showed similar results for HbsAg positivity among blood donors, considered as generally healthy, where they were observed for antigenemia up to three days post vaccination, after which they turned

negative.⁽¹¹⁾ Another study on blood donors by Dow BC et al also disclosed that HBsAg disappeared five days post vaccination.⁽¹²⁾ However, some studies are in contrast with the current study findings of HBsAg positivity turning negative one week post vaccination. This might be as previous studies were conducted on hemodialysis patients and healthy infants. Lately, Rysgaard CD et al found 11 patients to be HBsAg positive from a large number of patients presenting at an academic institute attributed to the vaccine, no positive results were seen beyond 14 days.⁽¹³⁾ Olde C et al has reported HBsAg positive results as 50% among hemodialysis patients and concluded that it lasted no more than two weeks.⁽¹⁴⁾ Few case reports among infants also showed prolonged antigenemia that became negative 18 and 28 days post vaccination.^(4, 5, and 7)

There is literature discussing the variation in outcome due to the method of immunoassay for HBsAg and the type of hepatitis B vaccine administered. The case report of a female dialysis patient by Onuigbo et al demonstrated that she remained negative after receiving Recombivax (Merck) vaccine, although she became positive subsequent to Engerix B (Glaxo SmithKline) vaccine booster that turned negative after one week.⁽¹⁵⁾ Lunn ER et al in a case report revealed that 18 days post vaccination with Engerix B, blood donation was deferred due to positive HBsAg, which was then attributed to the vaccine.⁽¹⁶⁾ These studies are in comparison with the present study where Engerix-B has been used from Glaxo Smith Kline Beecham. Another aspect of study by Dow BC et al was that different immunoassay methods were utilized for HBsAg, they inferred that antigen reactivity depends on the diagnostic assay used.⁽¹²⁾ Zaiee M et al in a clinical trial among healthy adults has also postulated that HBsAg positivity depends on the type of vaccine and the diagnostic testing technique.⁽¹⁷⁾ On the contrary, Otag F in a clinical trial with different brands of Hepatitis B vaccine deduced that vaccine induced antigenemia could be a possibility with any kind of HBV administered.⁽¹⁸⁾

The exact mechanism by which HBsAg false positivity could have occurred has not been highlighted in earlier studies. It has been

postulated that differences in tissue absorption, body composition, and blood flow in muscle might affect the plasma concentration of vaccine antigen. It has also been suggested that transient HBsAg positivity might result from early, slow, variable absorption of the vaccine antigen from the muscle.⁽⁸⁾

Conclusion:

This study highlighted that vaccine induced HBsAg reactivity is a constant problem that is difficult to eliminate. It can be a challenge if the patient is not followed up and he presents later to same hospital or to another hospital, when his results could be negative, due to diverse diagnostic techniques or the time interval post vaccination. This study confirmed that HBsAg reactivity might be seen in regular screening programs for healthy adults. Therefore, caution should be observed to avoid apprehension among healthy adults due to the stigma and the chronic nature of the disease. In addition, the high cost involved in assessing these healthy adults for hepatitis B infection could also be avoided by appropriate history and proper counseling.

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