Current characteristics of chronic hepatitis B in Egypt
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Background and aim
In the era of hepatitis C virus eradication, Egypt had to pay attention to the two million infected with chronic hepatitis B. This study aimed to observe the current characteristics of chronic hepatitis B virus (HBV) infection in Egypt.

Patients and methods
This cross-sectional study was conducted on 183 patients with chronic HBV infection. The demographic, epidemiologic, clinical, laboratory, and treatment data were collected from patient registries.

Results
Positive hepatitis B e-antigen (HBeAg) cases represented 18.04%. They were younger (31.09±8.542 – 38.22±10.6 years) (P<0.05), with higher alanine aminotransferase (84.91±67.855 – 53.75±55.575 U/l) (P<0.05) and viral loads (3.58×10⁸±16.49×10⁸ – 1.74×10⁶±10.1×10⁶ IU/ml) (P<0.05), particularly in chronic active carrier states. Unsafe hygienic procedures (sharing toothbrushes and razors) were the main infective routes (73.7%). Coinfection with hepatitis C virus was documented in 14.7%, along with 16.3% with schistosomal infestation. HBV and hepatitis D virus coinfection was reported in 8.9% of the studied cohort. Radiologically, liver cirrhosis was detected in 44% of cases, with associated splenomegaly in 20.7%. Histologically, 40.2% were found to have significant pathology (A2, F2>). Thirty (16.3%) cases were outside international guidelines of treatment, only for follow-up. Overall, 70.5% were subjected to lamidine therapy, with unfair responses mainly detected in the HBeAg-positive group (71.4%), who responded marvelously to interferon finite regimens. HBeAg-positive status and schistosomiasis were found to be associated with poor response to oral antivirals by multivariate analysis (P<0.05).

Conclusion
More classified governmental censorship efforts, notably on private organizations, along with awareness levitation are promptly mandated. Additionally, the poor response to oral antivirals in HBeAg-positive patients signifies sticking to interferon as a first-line treatment option.

Keywords:
alanine aminotransferase, characteristics, Egypt, hepatitis B e-antigen, hepatitis B virus, regimens and periodical follow-up for biochemical, virological, and e-antigen seroconversion

Introduction
Egypt is burdened with approximately two to three million chronic hepatitis B (CHB)-infected personnel. Individuals with CHB are at increased risk of developing serious problems including liver cirrhosis, hepatic decompensation, and promptly, hepatocellular carcinoma (HCC) [1]. Management of CHB in Egypt is complex with many intermingled clinical, economic, social, and cultural conditions, along with the generally poor compliance to both follow-up and treatment strategies.

The predominant hepatitis B virus (HBV) genotype in the Mediterranean area including Egypt is genotype D, which is more often associated with hepatitis B e-antigen (HBeAg)-negative variants with more severe liver disease [2].

The HBeAg-negative variant is highly prevalent in Egypt, representing a late phase of HBV infection characterized by persistent viral replication, progression of liver disease, and early development of cirrhosis [3]. The most recommended treatment for the minority of patients with HBeAg-positive CHB is 48-week course of PEG-interferon (IFN),...
with the best chance of anti-HBe seroconversion, which is frequently used as a primary end point, as it was associated with increased survival and a reduced risk of developing HCC [4].

Lack of epidemiological studies concerning HBsAg-positive Egyptian patients, along with unresolved questions about their clinical characteristics, lines of treatment, and treatment outcomes, was the motivations to carry out this study.

**Patients and methods**

This observational cross-sectional study was conducted on Egyptian patients with CHB coming to the outpatient virology clinics of Hepatology Department, National Liver Institute (NLI), Menoufia University, Egypt, from January 2013 till December 2014.

**Inclusion and exclusion criteria**

Egyptian patients with CHB infection (persistent positive HBsAg >6 months with positive HBV DNA by PCR) were enrolled [5,6]. Individualized written informed consent, along with the approval of the NLI ethical committee, was a prerequisite before enrollment. Coinfection with hepatitis C virus (HCV) and hepatitis D virus (HDV) were not exclusion standards. However, concomitant autoimmune or any other liver disease cases were excluded.

All procedures performed in the study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Approximately 319 patients with chronic HBV infection were primarily recruited in this study. However, only 183 patients were enrolled owing to their complete demographic, clinical, and laboratory data, as well as at least 2-year treatment response follow-up data. Collected data included the following:

1. Demographic data included age, sex, BMI, speculative mode of transmission, medical history, and the presenting symptoms.
2. Laboratory tests comprised liver function tests, including bilirubin (total and direct), albumin, aspartate aminotransferase (AST), and alanine aminotransferase (ALT), and prothrombin time. HCV and HDV antibodies detection and testing for HBV DNA using PCR, as well as indirect hemagglutination (IHA) for schistosomiasis were also done.
3. Abdominal ultrasonography was done for detection of cirrhosis and/or HCC.
4. Liver biopsy was done whenever indicated, with histological evaluation according to Metavir scoring systems [7].
5. Treatment regimens and periodical follow-up for biochemical, virological, and e-antigen seroconversion.

**Statistical analysis**

Data were statistically analyzed using statistical package for the social science program, version 13 (version 20; Inc., US, Chicago, IL), for Windows, and for all the analysis, a P value less than 0.05 was considered statistically significant: Data are shown as mean, range, or value and 95% confidence interval and frequency and percent. χ² test was done for qualitative variable analysis. Analysis of variance test was done to compare three variables. Kruskal–Wallis test was done to compare three or more variables. Tamhane test is a post-hoc test, and it was done for variables of significant difference of more than two groups. Spearman’s correlation test was done to study correlation. Multivariate analysis was carried out with the logistic binary regression.

**Results**

This study was conducted on 183 patients with chronic HBV. They were classified according to HBeAg status into two groups: group I included 150 (81.96%)

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### Table 1 Demographics and laboratory data of the patients

<table>
<thead>
<tr>
<th>Variables</th>
<th>Groups</th>
<th>Means±SD</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>Group I</td>
<td>38.22±10.6</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td></td>
<td>Group II</td>
<td>31.09±8.542</td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>Group I</td>
<td>28.9±7.79</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td></td>
<td>Group II</td>
<td>26.76±6.89</td>
<td></td>
</tr>
<tr>
<td>Sex (males) [n (%)]</td>
<td>Group I</td>
<td>114 (76.0)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td></td>
<td>Group II</td>
<td>26 (78.8)</td>
<td></td>
</tr>
<tr>
<td>AST (U/l)</td>
<td>Group I</td>
<td>46.17±34.467</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td></td>
<td>Group II</td>
<td>61.58±45.899</td>
<td></td>
</tr>
<tr>
<td>ALT (U/l)</td>
<td>Group I</td>
<td>53.75±55.575</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td></td>
<td>Group II</td>
<td>84.91±67.855</td>
<td></td>
</tr>
<tr>
<td>Basal viral load (IU/ml)</td>
<td>Group I</td>
<td>1.74×10^6±10.1×10^6</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td></td>
<td>Group II</td>
<td>3.58±108</td>
<td>±16.49×10^8</td>
</tr>
</tbody>
</table>

ALT, alanine aminotransferase; AST, aspartate aminotransferase.
patients with negative-HBeAg, and group II included 33 (18.04%) patients with positive-HBeAg. Demographic and laboratory baseline data are tabulated in Table 1.

Accidental discovery of infection was reported in 89.3%. Jaundice was a primarily presentation in only seven (4.7%) patients. Otherwise, fatigue, lower limb edema, and right upper quadrant abdominal pain were the presentations of minor occurrence. Regarding possible routes of infection, 135 (73.7%) patients had a history of unhygienic attitudes, such as sharing toothbrushes and shaving razors. Surgical operations and dental procedures as a risk factor were reported in 13.1% of cases. Blood transfusion had been documented in 2.7% of cases. No history of drug abuse or abnormal sexual behavior was reported (Table 2).

IHA of schistosomiasis was found to be significantly positive in 20 (13.3%) patients and 10 (30.3%) patients in groups I and II, respectively ($P<0.05$). HCV antibodies were found positive in 25 (16.7%) and two (6.1%) patients in groups I and II, respectively ($P<0.05$). Only 85 (46.4%) patients were surveyed for HDV antibodies and were found to be positive in three (4.9%) patients in group I and four (16.7%) patients in groups II ($P<0.07$) (Table 3).

Univariate analysis proved ALT levels and positive HBV DNA PCR were the only determinants of cirrhosis occurrence ($P<0.05$); however, multivariate analysis had negated this postulation ($P>0.05$).

Lamivudine was used in treatment of 115 (76.7%) patients in group I and 14 (42.4%) patients in group II. Entecavir was used in treatment of nine (6.0%) patients in group I and three (9.1%) patients in group II. IFN was used in treatment of one (0.7%) patient in group I and nine (27.3%) patients in group II. Tenofovir was used in treatment of one (0.7%) patient in group I and one (3.0%) patient in group II. Only 30 (16.4%) patients had undergone follow-up without treatment (Figs 1 and 2).

Regarding predictors of treatment response, multivariate analysis showed that presence of HDV and schistosomiasis were the independent predictors of poor treatment response ($P<0.05$) (Table 4). Poor

### Table 2 Possible routes of infection

<table>
<thead>
<tr>
<th></th>
<th>HBeAg</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Negative</td>
<td>Positive</td>
</tr>
<tr>
<td>Past history of unhygienic procedures in brushing teeth and shaving [$n$ (%)]</td>
<td>110 (73.3)</td>
<td>25 (75.8)</td>
</tr>
<tr>
<td>Past history of blood transfusion [$n$ (%)]</td>
<td>4 (2.7)</td>
<td>1 (3.0)</td>
</tr>
<tr>
<td>Past history of surgical operations [$n$ (%)]</td>
<td>23 (15.3)</td>
<td>1 (3.0)</td>
</tr>
</tbody>
</table>

HBeAg, hepatitis B e-antigen.
response for oral antiviral treatment was detected in patients with positive HBeAg status along with schistosomiasis ($P<0.05$) (Table 4).

Only three cases of HBV-related HCC were discovered during the course of the study.

**Discussion**

The higher prevalence HBeAg-negative CHB is mimicking the mainstream of HBV cases all over the world [8,9]. Many countries have sincerely devoted a lot of studies for analyzing their national characteristics of patients with CHB stressing on the HBeAg status: in 2012, a Saudi Arabian study performed by Abdo et al. [10] had estimated a less than 5% prevalence of HBeAg positivity. An American study by Widjaja et al. [11] had 34% of their cohort to be HBeAg positive. Two Brazilian studies have been reported: first was done in 2009 by Tonetto et al. [12], which declared that 70% of HBsAg-positive patients were HBeAg negative, whereas the second was done by Chachá et al. [13], with more inclination toward the HBeAg-negative verge. An Iranian study had pondered the local magnitude of HBV infection on tight spot to be astonishingly more than 98% of cases to be HBeAg negative [14]. In Oman, 96% of patients with CHB had negative e-antigen status [15]. In France, Greece, Italy, Portugal, and Spain, studies had demonstrated a similar pattern of domination of negative e-antigen HBV cases [16–21].

In Egypt, the current picture of HBV infection characterization is yet lacking [22]. Although it was reported in 2007 that 81% of Egyptian patients were HBeAg negative, a ratio of 90–95% was reported by the same author in 2009 [2–23]. Saudy et al. [24] had reported that HBsAg disappears early in patients with HBV genotype D, which is the predominant genotype in Egypt. This occurs due to mutations in the precore and/or basic core promoter regions of the genome that abolish or diminish the production of HBeAg [9]. However, no studies were targeted just to categorize chronic HBV Egyptians.

In this study, concerning HBeAg status, 150 (82.4%) patients were found with negative HBeAg and 33 (17.6%) with positive HBeAg status. These results are supported by the hypothesis of Chachá et al. [13], who documented the increase in the proportion of HBeAg-negative cases over the past 15 years, reflecting a greater circulation of mutant viruses. However, the fact that HBeAg-negative patients subjected to antiviral treatment were not excluded from this study should be taken into consideration, with the possibility of bias in the data obtained owing to the presence of patients in whom seroconversion of the HBeAg was induced by medications. On the contrary, in spite of the statement that most patients in this study were HBeAg negative (82.4%), the slight tilt of increase in HBeAg-positive cases (17.6%) at the expense of HBeAg negative ones cannot be denied. Dissimilar to previous studies on Egyptians [2], these deviations might suggest a starting alteration in HBV HBeAg configuration. This hypothesis is supported by a recent Egyptian study conducted by Fouad et al. [25] who nominated 81.9% of their chronic HBV cohort to be HBeAg negative. Improved viral hepatitis screening (premarital and preemployment) along with better diagnostic modalities might be the offenders of this new deviation.

In our study, most of the patients were mainly males and slightly overweight, whereas those with HBeAg negative were found to be older than those with positive HBeAg, which was expected as this is a later stage of infection. These results were highly supported by most studies [9,12,17,26,27]. All our patients in both groups were born before 1992, a fact which signified the efficacy of the Egyptian national compulsory HBV vaccination in infancy [22].

<table>
<thead>
<tr>
<th>Variables</th>
<th>B</th>
<th>SE</th>
<th>Wald</th>
<th>P</th>
<th>Exp(B)</th>
<th>95% CI for Exp(B) Lower</th>
<th>Upper</th>
</tr>
</thead>
<tbody>
<tr>
<td>For all patients</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Presence of HDV</td>
<td>−1.998</td>
<td>0.862</td>
<td>5.371</td>
<td>0.02</td>
<td>0.136</td>
<td>0.025</td>
<td>0.735</td>
</tr>
<tr>
<td>Presence of schistosomiasis</td>
<td>−1.289</td>
<td>0.629</td>
<td>4.205</td>
<td>0.04</td>
<td>0.276</td>
<td>0.080</td>
<td>0.945</td>
</tr>
<tr>
<td>For patients who received oral antiviral therapy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive-HBeAg</td>
<td>−1.809</td>
<td>0.711</td>
<td>6.472</td>
<td>0.011</td>
<td>0.164</td>
<td>0.041</td>
<td>0.660</td>
</tr>
<tr>
<td>Presence of HDV</td>
<td>−2.114</td>
<td>1.087</td>
<td>3.785</td>
<td>0.052</td>
<td>0.121</td>
<td>0.014</td>
<td>1.016</td>
</tr>
<tr>
<td>Presence of schistosomiasis</td>
<td>−1.433</td>
<td>0.721</td>
<td>3.947</td>
<td>0.047</td>
<td>0.239</td>
<td>0.058</td>
<td>0.981</td>
</tr>
</tbody>
</table>

B, estimated regression coefficients; CI, confidence interval; Exp(B), estimated odds ratio; HBeAg, hepatitis B e-antigen; HDV, hepatitis D virus; Wald, Wald $\chi^2$. Table 4 Multivariate logistic regression of predictors of poor treatment response.
Analyzing the modes of infection was found to be predominantly horizontal transmission, corresponding with the Egyptian study piloted by Elzayadi [23]. These results are mainly exemplified by the improper sterilization techniques, especially in the private health care sector, a contempting sign of the poor governmental exertions concerning the robust formal private center censorship. No one also can deny the contribution of the improper personal hygienic measures practiced by the mostly low socioeconomic Egyptians to this issue. Again, another ominous sign of the humble underprivileged administrative inputs at awareness levitation of the inhabitants’ health education, added to the disfavored socioeconomics.

Disgrace and dishonor conjoined with drug abuse and abnormal sexual behaviors had omitted these two possible routes of HBV infection from the list of studied cohorts.

On studying liver function tests, both transaminases (ALT and AST) were high and significantly higher in the positive HBeAg group. Moreover, ALT level was found to be above twice the upper limit of normal likewise in those with positive HBeAg than the other group. These results are in agreement with Yang et al. [28] who conducted a large Chinese study, with evidence of higher ALT levels in patients with HBeAg-positive CHB than those with HBeAg-negative CHB. Moreover, Cacoub et al. [29]; Pungpapong et al. [30]; and Elgouhari et al. [31], had determined these postulations, advocating the elevation to an immune reaction for viral clearance. Conversely, Bahramali et al. [32], had specified patients with HBeAg-negative CHB with superior levels of ALT, AST, and bilirubin.

With respect to serum bilirubin, albumin, and prothrombin time values in our study, no significant differences were recorded between our two groups. This comes in agreement with what was reported by Keshvari et al. [33] in their study.

With respect to viral load, higher values in patients with HBeAg-positive CHB than those with negative HBeAg ones were seen. Again, this was in correspondence with the Iranian study that had reported that higher serum HBV DNA was prevalent in most HBeAg-positive patients [33–36].

In our study, patients with HBeAg-positive CHB were found to be more vulnerable to schistosomal parasitic infestation according to the IHA test of schistosomiasis. It was found to be positive in 13.3 and 30.3% in groups I and II, respectively. These levels are different from those conveyed by Shiha et al. [37] who stated that 15.7% of HBV Egyptian patients were positive for schistosomiasis by the IHA test. As far as we know, there are no recent studies elucidating the actual current Egyptian load of schistosomiasis totally or in between HBV-infected patients. In spite of being unexplained, the higher prevalence of schistosomiasis coinfection with HBeAg-positive CHB patients can be a contributing factor yielding to more severe fibrosis and cirrhosis but not elevated transaminases and viral load.

Egypt which is profoundly burdened with HCV infection, a ratio of 14.75% of HBV/HCV coinfection is expected with the lower predilection in the HBeAg-positive group (6.1–16%). These data eliminated any role of HCV infection in the severity of liver disease in the HBeAg-positive group. An invariant route of infection of both viruses might be suggested; however, this supposition cannot be guaranteed.

In this context, the ratio of coinfection was 16% in an Indian study, 1.7% in an Egyptian one, 1.7% in a Brazilian study, 2.6% in a Turkish one, and 10–15% in Spanish, Italian, Japanese, Taiwanese, and Iranian studies [38–48]. Approximately 2–10% of those with HCV coinfection were HBsAg positive. The information on the treatment of this subset is scanty, but it seems reasonable that a first-line therapy could be peg-IFN plus RBV with the addition of or a shift to a high potency and high genetic barrier nucleos(t)ide analog for patients with HBV DNA persistence. HBV/ HCV-coinfected patients are under treatment evaluation following direct antiviral therapies of HCV [49].

In our study, only 85 patients had been tested once for HDV antibodies, and seven (8.24%) patients were found to be positive. This is consistent with Gish et al. [50] in an American study reporting that 8% of patients with CHB were confirmed to be HDV-coinfected. In other parts of the world, the seroprevalence of HDV among HBsAg-positive cases was 1.5% in Yugoslavia [51], 1.6% in Spain [52], 2.2% in Taiwan [53], 4% in Mexico [54], 16.6% in Pakistan [55], 24.4% in Bangladesh [56], 12.5% in Russia [57], 83.3% in Romania [58], 23.6% in Japan [59], and 8.3% in Italy [60]. These studies suggest that the prevalence of HDV differs in various parts of the world and is higher in Eastern Europe and western Asia. HDV was more prevalent in the positive HBeAg status (16.7–4.9% in the negative group). Fouad et al. [25], had labeled Delta
infection to be prevalent with negative HBeAg status, highlighting its role in HBV replication reduction. Treatment with IFN-alpha might be an acceptable option in some cases [61].

The classification of CHB, defined by European Association for the Study of the Liver, was found to affect natural history rather than treatment strategies [62]. Consequently, we followed the American Association for the Study of Liver Disease practice guidelines regarding the diagnostic criteria. In brief, inactive carriers had persistent HBV infection without significant necroinflammatory disease. Chronic hepatitis was defined as HBsAg positivity with or without the presence of HBeAg and a high HBV DNA (>2000 IU/ml for HBeAg negative and >20 000 IU/ml for those with HBeAg positive), persistent or intermittent elevation in the serum ALT levels, and compatible liver biopsy. Liver cirrhosis was confirmed by abdominal ultrasound examination, fibroscan, and liver biopsy [6,32].

Accordingly, our two cohorts were categorized under these titles to chronic hepatitis and cirrhosis. Most HBeAg-positive patients were cited in the chronic hepatitis category (72.7%). They were younger (28.29±6.018 years) with higher serum levels of both ALT and basal viral load. Our patients with positive HBeAg status became cirrhotic at younger ages than the negative group (36.80±9.834 years vs. 47.79±9.291 years), with higher serum AST and HBV DNA. Consequently, in spite of being mostly chronic hepatitis, HBeAg-positive patients should be considered ‘cirrhotic to be’ and substantially treated as they are going to advance briskly at younger ages. Our results might be a continuation to what was mentioned in many studies [63–66]. However, others had reported higher rates of cirrhosis in the HBeAg-positive group [13,64]. On the contrary, Liu and colleagues, and Keshvari et al. [33], had questioned the effect of either states of HBeAg on the occurrence of liver cirrhosis. Collectively, there is no worldwide consensus regarding the influence of the HBeAg on the progression to cirrhosis [33,67].

Patients with significant fibrosis or cirrhosis, with either positive or negative HBeAg, should be considered for antiviral therapy [68]. Early detection of patients with significant hepatic pathology (fibrosis≥2 and/or activity≥2) with the immediate appropriate treatment can prevent the progression to end-stage liver disease and HCC development [69]. A profoundly depressive notification was narrated during follow-up of our patients with abdominal ultrasonography; three (1.64%) patients with liver cirrhosis had developed HCC, which was ascertained by abdominal triphasic computed tomographic scan. The three were HBeAg-negative patients. Correspondingly, many studies had negated any role of HBeAg status as a risk predictor of HCC development in chronic HBV infection [67,70]. Two patients were males with one female. The mean age of these three patients was 48 years old, and their mean BMI was 27.9 kg/m². They are all Child C class of the Child–Pugh classification of cirrhosis. Their mean serum transaminases were elevated along with basal viral load (two patients had basal viral load was <2000 IU/ml, while one was >2000 IU/ml). HCV coinfection was prevalent in two cases, denoting the impressive role of this coinfection in accelerating the fated carcinogenic process. However, relying on HCV antibody on diagnosis of chronic HCV is not ultimate. There is a usual anticipation in chronic HBV natural history especially in cirrhotic males above 40s as detected in the study of Li et al. [70]. In our study, the occurrence of HCC only in the HBeAg-negative cohort does not exclude or confirm the probability of HCC occurrence in the HBeAg-negative patients. The small-sized sample along with the limited number of HCC cases did not merit a justified statistical analysis.

Being costly, HBV genotype testing is not recommended to be routinely done for patients with chronic HBV [29]; accordingly, it was not done for all patients included in the study.

Accurate estimates of HBV viral load were done through quantitative HBV DNA testing which is critical to guide treatment decisions, including initiation of treatment and assessment of patient response. Quantitative detection of HBsAg also helps to manage patients receiving peg-IFN therapy; however, it is not recommended for routine testing in all international guidelines of HBV management [33]. Being a dynamic disease, untreated patients should be tested regularly to clarify indications for treatment. The goals of HBV treatment are to achieve virological and biochemical response and/or delay or arrest in the progression of liver injury and development of cirrhosis and HCC. Patients with HBeAg-negative chronic HBV require a longer duration for eradication than those with HBeAg-positive, particularly when oral treatment is used [71].

Being economic, with higher grades of safety and efficacy, lamivudine had been used in a country with restricted reserves like Egypt with distinguished rates
of acceptance. Lamidine monotherapy has been shown to benefit both patients either with HBeAg-positive or HBeAg-negative CHB [72,73]. In spite of lower rates of resistance along with higher efficacy, adefovir or entecavir had shown limited share in the HBV Egyptian market for their high cost.

In the current study, lamivudine was used in treatment of 129 (70.5%) patients of the total number of patients included in the study, of them 14 (42.5%) patients were HBeAg-negative patients. Entecavir was used in treatment of 12 (6.6%) patients of the total number of patients included in the study, where three (9.1%) patients were HBeAg-negative patients, whereas IFN was used in the treatment of 10 (5.5%) patients of the total number of patients included in the study, of whom one (0.7%) patient had negative HBeAg (had dual infection with chronic HCV) status, and nine (27.3%) patients were HBeAg-negative patients. Tenofovir was used in treatment of only two (5.5%) patients of the total number of patients included in the study, where one patient was HBeAg-negative (0.7%) and the other was HBeAg-negative (3.0%).

Thirty (16.4%) patients of the total number of patients included in the study were not eligible to treatment according to EASL guidelines and were followed-up; of them, six (18.2%) patients were HBeAg-positive (inactive carrier states).

After 2-year treatment follow-up, our HBeAg-positive cohort had shown the lowest response rates (71.4% were nonresponders). Combined lamivudine and adefovir were used in the treatment of 6 HBeAg-positive patients. Tenofovir was used in four patients; one of them was HBeAg-positive. Entecavir was used in the treatment two HBeAg-positive patients, whereas IFN was used in the treatment of one HBeAg-positive patient. In our study, 90.4% (104 of 115 patients) of patients with HBeAg-negative CHB had good response to lamivudine, whereas only 28.6% (four of 14 patients) of HBeAg-positive CHB patients had good response to lamivudine. Paik and colleagues reported that 86.0% of HBeAg-negative CHB Korean patients showed good response following 24 months course of lamivudine therapy [74,75].

Viral resistance testing is not recommended for antiviral treatment patients. Viral resistance testing is beneficial for patients who have been treated with antiviral drugs, who have been treated with nucleoside (acid) analogs, who have persistent viremia, or who have undergone virological breakthroughs during treatment.

The classification of our cohorts according to HBV DNA and ALT had unveiled a catastrophic manipulation of chronic HBV patients with normal ALT and low HBV DNA. Overall, 32% of them who were HBeAg negative and 50% of them who were HBeAg positive were subjected to antiviral treatment against all the international guidelines. We examined their histopathological data (which was not valid for all of them), and all were between F0 and F1. This unprofessional handling may predispose to both epidemiological and socioeconomic disasters.

Our study was a trial in mapping the HBeAg-positive CHB Egyptian patient characteristics. They were found to be mostly represented in the chronic hepatitis phase, usually with elevated liver enzymes and HBV PCR DNA serum levels. If they ever become cirrhotic, they are younger with more severe liver disease.

Conclusively, we heartily recommend more classified governmental efforts in HBV social awareness to limit the infectious resources. A more hard-hitting robust administrative censorship on the hygienic measures in health care organizations is needed, notably in the private sector. Establishment of an organization concerned with the notification of any incriminated or alleged resources of infection should be an infection control priority. Moreover, every patient with chronic HBV should be screened for Delta infection early on diagnosis and with every change in his clinical and laboratory data or treatment responsiveness. Enforcement of HBV screening program for the more susceptible groups – especially pregnant ladies – should be implicated, as most cases were discovered accidentally. In a country like Egypt with the highest HCV infection prevalence rates, it should be screened in every HBV-infected patient, as they had the same routes of infection. Treatment decisions should be precisely taken only whenever indicated according to the international guidelines. HBeAg-positive patients should be made to strictly stick to their treatment as they have cirrhosis at younger ages, with proper implementation of HCC screening in patients with chronic HBV, especially those with negative e-antigen.

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Conflicts of interest
There are no conflicts of interest.