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Prevalence of Hepatitis B Infection in Rheumatoid Arthritis Patients

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Abstract: Rheumatoid arthritis is a progressive and destructive inflammatory disease of the joints. They had increased mortality depend to use of immunosuppressive drugs. Hepatitis B virus infection is also a health problem in the world. Iran is moderate prevalence endemic area for Hepatitis B virus and it is come too reduced recently by children vaccination. Aim of this study is determined prevalence and screening of Hepatitis B virus infection in rheumatoid arthritis patients. This study is a descriptive cross-sectional which all patients with rheumatic arthritis recruited to study in Tehran in 2012. Then HbsAg and HbcAb assayed for each subjects. In 268 rheumatoid arthritis patients which (82.2%) were female and the average age is 46±14 years old. HbsAg and HbcAb were positive in 4(1.49%) and 9(3.35%), respectively. Only between duration of rheumatoid arthritis and HbcAb had significant association ($p<0.014$). The present study highlights Rheumatoid arthritis patients treated with immunosuppressive drugs are at increased risk to reactivation of hepatitis B virus, so screening for Hepatitis B virus infection should be performed prior to immunosuppressive therapy.

Key words: HBV, RA, screening, immunosuppressive HbsAg

INTRODUCTION

Rheumatoid arthritis is refractory and progressive inflammatory disease of the joints that is associated mainly with synovial hyperplasia (Mandl *et al.*, 2011). Incidence is common in the fourth and fifth decades of life and it is more common in women (Stammore *et al.*, 2013). Rheumatology clinical criteria suggest as morning stiffness more than one hour for six weeks, more than three symmetrical joints involvement, rheumatoid nodules and positive rheumatoid factor (Summers *et al.*, 2008).

Rheumatoid arthritis patients compared to healthy people had more other chronic diseases such as osteoporosis, infection, cancer, digestive diseases, allergies, vascular and heart disease, also they had increased mortality depend to used of immunosuppressive drugs (Kim and Kim, 2010).

HBV infection is a health problem in the world and 350 million people were carried this virus (Tan *et al.*, 2012). Iran is moderate prevalence endemic area (Ghorbani *et al.*,

2008) and it is come too reduced recently by children vaccination (Marusawa *et al.*, 2000; Ramalingam *et al.*, 2007).

Diagnosis of HBV infection is based on serologic markers such as HBSAg and HBC antibodies that positive before and approximately one month after the appearance of clinical symptoms (Roux *et al.*, 2006). When HbsAg was negative in widow period only diagnostic viral marker is HBC IgM Ab assay (Ramezani *et al.*, 2010). Some of the remedy whom used in rheumatoid arthritis caused immunodeficiency and caused reactive of latent hepatitis. Rituximab, abatacept as well as anti-TNF α should be used prudently in a patient with hepatitis because increased the risk of reactive hepatitis (Vassilopoulos *et al.*, 2010).

Immune-modulator medications as well as Immunosuppressive drugs for treatment of rheumatoid arthritis may be reactivating the occult hepatitis (Ghrensia *et al.*, 2012).

Considered to prevalence of hepatitis B virus infection in Iran and on other hand prevalence of

rheumatoid arthritis obligate uses of immunosuppressive drugs co morbidity of these two disease may be caused fulminant hepatitis (O'Brien *et al.*, 2007). Therefore, this study was design for evaluation of prevalence of hepatitis B infection in these patients.

MATERIALS AND METHODS

This evaluation is a descriptive cross-sectional study which all patients with rheumatic arthritis were referred to the rheumatology clinic in Baqiyatallah hospital at university of medical sciences of Baqiyatallah in Tehran in 2012.

Two hundred sixty eight rheumatoid arthritis patients recruited to study as census sampling after sign consent. Each persons completed prepared questionnaire form. Then from each subjects five ml blood sample take and centrifuged and separated its serum and refrigerated until ready for laboratory assy. Then HbsAg and HbcAb assayed by ELISA test of Diapro Kit manufactured in Italy country.

Exclusion criteria contain who that has a history of hepatitis, malignancies, uncontrolled diabetes, history of chemotherapy and HIV positive.

The Medical Ethics Committee approved this study and after described of aim for patients, study was done and if serology of hepatitis B virus infection was positive they guidance to treatment. In the end data analyzed by SPSS program 11.5 and statistical analysis was done as frequency test for prevalence, differences between the findings of the quantitative variances used Student-T test and discrepancy between the findings of qualitative testing with Chi-2-square analysis and significant level account as $p < 0.05$.

RESULTS

In this study, 268 rheumatoid arthritis patients were included that (82.2%) were female and the average age is 46 ± 14 (range 12-93) years old. The education level was 63.1% diploma and lesser and 87.7% was married. About 82.8% live in urban. Mean duration was 8.8 years and active rheumatoid arthritis was seen in 160 (59.70%) (Table 1).

Treatment of patients contain steroid in 160 (59.70%), azathioprin 51 (19.2%), methotraxate 203 (75.74%) and biologic drugs in 37 (13.80%).

HbsAg and HbcAb were positive in 4(1.49%) and 9(3.35%), respectively. Only between duration of rheumatoid arthritis and HbcAb had significant association ($p < 0.014$), other data are shown in Table 2.

Table 1: Demographic data of rheumatoid patients

Data	No.	Valid percent
Sex		
Female	215	81.7
Man	48	18.3
Education level		
>Diploma	89	41.8
Diploma	80	37.6
<Diploma	44	20.7
Marriage condition		
Married	235	92.9
Single	18	7.1
Living places		
Rural	12	5.1
Urban	222	94.9
Hepatitis in family		
yes	8	3.0
No	255	97.0
RA in family		
yes	63	24.0
no	200	76.0

Table 2: Involvement of joints, treatment and hepatitis B virus in RA patients

Variable	No.	Valid percent
Active RA		
Yes	160	59.70
No	108	40.30
Joint deformity		
Yes	99	36.90
No	169	63.10
No biologic therapy		
Yes	26	9.70
No	242	90.30
Biologic therapy		
Yes	37	13.80
No	231	86.20
HbsAg		
Yes	4	1.49
No	264	98.51
HbcAb		
Yes	9	3.35
No	259	96.65

DISCUSSION

Rheumatoid arthritis is a chronic disease of the joints accompanied by progressive destruction and had more mortalities than normal population especially if they treated by immunosuppressive drugs (Urata *et al.*, 2011). Other chronic disease such as HBV hepatitis accompanied with rheumatoid arthritis can increment their complication and it can reactive after begun of immunosuppressant drugs (Mori, 2011). Mortality and morbidity of RA patients infected with chronic hepatitis has increased, especially when they took immunosuppressive drugs, therefore before beginning of therapy screening of hepatitis B virus indicated (Manzano-Alonso and Castellano-Tortajada, 2011).

Iran is moderate endemic prevalence of HBV and vaccination in children reduced its prevalence recently (Ghorbani *et al.*, 2008) but these two diseases is health problem and may worse each other

(Alavian *et al.*, 2010; O'Brien *et al.*, 2007). DNA HBV assay is certainly assayed for occult hepatitis but this test did not do in this study because its cost don't provided (Tan *et al.*, 2012).

Some authors believed that biologic and non biologic drugs had not any risk so prophylaxis against HBV don't cost benefit and they counsel assay HBV DNA PCR quantitatively and even viral load is increased treated with antiviral (Ndongo *et al.*, 2011).

HBSAg is the best assay screening for HBV infection but it sometimes is negative and other marker such as HBCAb should be examined (Roche and Samuel, 2011).

Fulminant hepatitis may be occurring in RA patients after immunosuppressant therapy so DNA PCR assay is mandatory for detection of occult hepatitis (Watanabe *et al.*, 2012). Improved hepatitis is also at risk after immunosuppressive therapy especially by biologic drugs in RA (Chung *et al.*, 2009) and sometime required to use of entecavir for prophylaxis (Lan *et al.*, 2011).

In this study prevalence of HBCAb is 3.4% which more than prevalence of HBSAg so screening of HBCAb should be adds to HBSAg for meticulous evaluation of HBV infection in RA patients because isolated HBCAb positive is a risk factor for reactivation of hepatitis B virus (Tanaka and Urata, 2012).

Isolated positive HBCAb can be seen in three conditions that the first is acute infections, second chronic hepatitis which may be progressive and third improved and therefore type 1 and 2 after immunosuppressive therapy are at risk for reactivation and fulminant hepatitis (Lee and Weinblatt, 2001; Ryu *et al.*, 2012).

Patients who had HBCAb positive and treated with immunosuppressive drugs, reactivation of hepatitis may be occurred so evaluation every 6 month for hepatitis had indicated until don't delayed its prophylaxis (Lan *et al.*, 2011).

In this study HBCAb had significant association with long term of disease. Therefore RA patients with long duration time may be had more occult hepatitis than short duration which screening of HBCAb should be performed for them (Kim *et al.*, 2012). Although, prevalence of HBV infection in RA patients resemble to general population (Tanaka and Urata, 2012) but diminished immunity by old age and immunosuppressive therapy for RA may be increased risk of reactivation of HBV so screening was mandated in old age RA patients (Manzano-Alonso and Castellano-Tortajada, 2011).

Prior to Biologic and no Biologic drugs for RA such as anti TNF α , Methotrexate and abatacept which

can be reactive occult hepatitis, screening should be performed to prevent reactivation of HBV infection (Roche and Samuel, 2011).

In here RA was more prevalence in women resemble to other study but no any variant and demographic data had significant association with prevalence of HBV infection (Tamori *et al.*, 2011).

Limitation of this study was little budget for HBV DNA PCR viral load assay that it is more sensitive for detection of occult hepatitis in RA patients.

CONCLUSION

Prevalence of hepatitis B in patients with rheumatoid arthritis is similar to normal population but since these patients treated with immunosuppressive drugs are at risk of reactivation of hepatitis and so screening should be considered for them and if need, they be treated for HBV infection.

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