

Relationship Between Serum Iron Profile and Liver Density in Non-Enhanced CT-Scan

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Abstract- It is known that liver biopsy is the gold standard of diagnosing liver iron deposition. By considering liver biopsy complication and cost, introducing a method to restrict unnecessary biopsy or even an alternative for liver biopsy can be useful. This study examined the relationship between serum iron profile and liver density on CT-Scan without contrast material injection. In this study, 76 patients were referred from different Rasool-Akram Hospital parts in 2015-2016 (People who have undergone abdominal CT-scan for any reason, and blood tests included iron and lipid profiles). To calculate the liver mean density of a CT-scan, densities of 12 sites with an individual area of 1 cm² on 3 different sections of the liver were obtained, and their average was recorded. Data were analyzed by SPSS V.16 using Kolmogorov-Smirnov, independent T-test, and two-sample T-tests with a significance level of $P < 0.05$. There is a significant relationship between the serum iron and serum ferritin levels with liver density. By increasing TIBC levels, the difference between liver and spleen densities increases, but no significant correlation was found between TIBC level and liver density. Moreover, there was no relationship between serum iron levels and serum ferritin with the difference between liver and spleen densities. The evaluation of liver density may be an alternative to liver biopsy in some cases or at least can be considered to restrict unnecessary biopsies.

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Introduction

The amount of iron in the body is affected by various factors such as transfusion, iron in the diet, drinking alcohol, and blood loss during menstruation, pregnancy, and blood donation. Also, the amount of iron in the body indirectly leads to changes in the level of blood iron profiles, including TIBC, serum iron, and ferritin (1,2). Some diseases and pathological conditions, including hemochromatosis, taking high-doses of iron for a long time, or chronic anemia, such as thalassemia associated with frequent blood transfusions because of an increase in the iron input leading to excess accumulation of iron in the body. Too much accumulation of iron can lead to tissue damage and dysfunction in several organs. These disorders are also related to greater levels of iron and iron-containing products like ferritin in the serum. Liver is the most important organs affected by the accumulation of excess iron, in which this iron is stored as ferritin (3). Results of an increase in the content of liver iron are morphological changes and parenchymal

damage that eventually leads to liver fibrosis.

To prove these changes in the liver, we need a biopsy and liver biopsy can provide valuable information to determine the stage of the disease (severity of inflammation and liver cell damage), prognosis, and also helping the physician find the most effective treatment and disease management (4-9). On the other hand, the liver density that can be measured by CT scan elevated in cases of iron overload in the liver (10,11). According to the abundant blood supply of the liver and being rich in reticuloendothelial tissue (which is the site of iron storage), the reason for this is justifiable (2). Typically measuring the concentration of serum ferritin is used to determine body iron content (12). Because excessive iron is stored as ferritin in a healthy person, by using the formula that one microgram of serum ferritin is equivalent to 8 to 10 mg of stored iron, the amount of total iron storage is estimated (13-15).

Considering the importance of this issue, there are different ways to achieve a level of iron overload in

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Iron profile-liver density relationship in CT-scan

patients with liver dysfunction, including ferritin levels and liver biopsy, as discussed above. In order to obtain a non-invasive method instead of a liver biopsy, this study was to evaluate the relationship between serum iron profile levels with liver density on CT scan without injection of contrast medium.

Materials and Methods

This cross-sectional study was conducted on 76 patients (the sample size was obtained from the Cochran formula) referred from different parts of Rasoul-e-Akram Hospital in 2015-2016 and had the criteria for entering the study (people who have undergone abdominal CT scan for any reason, blood tests included iron and fat profiles and liver ultrasonography examination during the past 30 days). Exclusion criteria were the presence of artifacts in CT scan images as accurate measurements of the liver densities were not possible (these artifacts included Beam Hardening due to patient's hands position or the motion artifact), the presence of simultaneous hyperlipidemia as it also reduces the density of the liver or any grade of fatty liver change on liver ultrasonography examination. Then, after obtaining informed consent, patients were assured that all their information would remain confidential. The collection pool in this research was data of the central laboratory and radiology department of Rasoul-Akram Hospital. In this study, blood tests and abdominal CT scan were done in one day (to avoid temporal effects on iron levels or CT densities) to improve the accuracy.. The CT scan of patients was analyzed in the MARCO PACS software used in the radiology department and the mean CT scan density of liver was obtained as follows: the density of 12 sites with an individual surface area of 1 cm² in 3 sections of liver avoiding the vessels were obtained and their mean was recorded as mean hepatic density (MHD). Also, the density of 6 sites with an individual surface area of 1 cm² in 3 sections of splenic tissue was obtained, and they are mean recorded as mean splenic density (MHD) as a reference point, and difference between the mean of the liver density and spleen density (MHD-MSD) was recorded as another criterion for comparison with serum iron profile laboratory data (12).

Then, a potential relationship between serum iron profile and liver density on non-enhanced CT scan were analyzed by using SPSS software version 16 and Kolmogorov-Smirnov tests, independent t-test, and chi-square test with a significant level of $P < 0.05$.

Results

In this study, 76 patients were investigated. Of these, 42.1% were male and 57.9% were female. The mean age of the patients was 53-year-old, with 15.8% of patients between 21 and 30-year-old, 26.3% between 31 to 40 years, 10.5% between 61 and 70 years, 31.6% between 71 and 80 years, and 3.5% of the patients were over 80-year-old. Patients aged 71 to 80 years had the highest percentage.

The results of this study between serum iron levels and liver density on non-enhanced CT-scan in the samples examined showed a significant relationship ($P=0.03$).

However, regarding the study of the relationship between serum TIBC level and liver density on non-enhanced CT-scan in the samples, there was no statistical significance ($P=0.757$) (>0.05).

As well, the results of the investigation between serum ferritin levels and liver density on non-enhanced CT scans were statistically significant ($P=0.019$).

Our results indicate that there was no statistically significant relationship between serum iron levels and MHD-MSD on non-enhanced CT scans ($P=0.101$) (>0.05). The results of the analysis between serum TIBC and MHD-MSD showed a statistically significant relationship ($P=0.046$). Also, there was no significant relationship between serum ferritin levels and MHD-MSD in the sample ($P=0.136$) (>0.05).

As well, the results of this study showed that among the levels of MHD, MHD-MSD, serum iron, serum ferritin, and TIBC in both women and men are not statistically different. Also, the amount of serum TIBC, serum iron and MHD levels in both aged over 55 and less than 55 years are not different. While MHD-MSD and serum ferritin levels in both groups are different so that the mean of serum ferritin levels in people over 55 years is higher than those less than 55 years. The levels of MHD-MSD, like ferritin levels, in people older than 55 years, are higher than people less than 55 years.

Discussion

In some diseases such as hemochromatosis, which are associated with impaired intestinal absorption of iron or multiple transfusions, iron deposition in the liver happens that is related to its parenchymal damage. The main method for proving the existence of these changes and damage is the liver biopsy, but the biopsy technique is painful, expensive, and invasive. On the other hand, liver density, which can be measured by CT scan, can

indirectly indicate the hepatic iron overload. In some cases with clear signs of iron accumulation whose serum ferritin level is incorrectly estimated low, high-density liver reveals the possibility of wrong ferritin levels (11,17). In this study, the relationship between serum iron profiles with liver density on a non-enhanced CT scan was investigated and showed a significant relationship between the serum iron and ferritin levels with liver density; so that by increasing these serum levels, higher liver density is expected. Therefore, by measuring and monitoring liver density in the diseases with accompanying iron overload, one can estimate the degree of iron accumulation in the liver. Moreover, the level of MHD-MSD and serum ferritin levels are different in both groups aged over 55 and less than 55 years, which can be attributed to an increase in iron accumulation in older ages.

Non-invasive imaging techniques such as MRI have also been used to monitor the accumulation of hepatic iron. As well, a systematic review by Paul and Sijens (2010) about the determination of the liver iron content by MRI was performed. They concluded that MRI is a useful and non-invasive method that can be used to investigate the liver iron content (12). Therefore, according to the previous results, MRI is a non-invasive method, done directly, and not be influenced by other disorders (18).

The advantages of using a CT scan is the short time of its implementation, its low price, and the need for less patient cooperation, but on the contrary, the patient is exposed to ionizing radiation from the CT scan. Further studies are required to compare a non-enhanced CT scan and T2*MRI for monitoring liver iron accumulation. In addition, more research is needed to explain the exact level of liver density or MHD-MSD above which pathologic hepatic iron accumulation is considered and different classification such as mild, moderate and severe hepatic iron overload based on CT densities may be suggested.

In conclusion, the findings of the present study suggest that there is a significant relationship between serum ferritin levels and serum iron levels with liver density on non-enhanced CT-scan. Therefore, to determine the amount of liver iron deposition in patients afflicted with iron overload especially when there is a need for frequent monitoring, perhaps instead of liver biopsy, serial measurement of hepatic density can be used, which compared to other non-invasive methods such as T2*MRI is faster, cheaper and with less need for patient cooperation, but on the contrary, the patient is exposed to ionizing radiation from the CT scan.

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Iron profile-liver density relationship in CT-scan

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