

Frequency of Hypothyroidism in Patient With Hepatitis C Infection Attending A Tertiary Care Hospital

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ABSTRACT

Objective: To determine the frequency of Hypothyroidism in patient with Hepatitis C infection

Study Design: Cross sectional study

Place and Duration of Study: This study was conducted at the Department of Gastroenterology, Liaquat National Hospital, Karachi from Oct 2018 to April 2019.

Materials and Methods: All patients who met the inclusion criteria and visited the Department of Gastroenterology at Liaquat National Karachi Hospital were included in the report. After acceptance by ethics and informed and written consent. Brief history was taken, clinical examination was done and blood sample was sent for Thyroid stimulating Hormone (TSH), free T4 (FT4) to access the outcome i.e. frequency of Hypothyroidism in patient with Hepatitis C infection.

Results: 97 patients with Hepatitis C infection were included. 46 patients of which were (i.e., 47.4%) males & 51 patients (i.e., 52.6%) were female patients with the age of 33.96 ± 7.247 years. Hypothyroidism was seen in 25 patients (25.8%).

Conclusion: In 25.8 percent of patients with HCV infection, HCV infection itself induces biochemical thyroid dysfunction prior to treatment.

Key Words: Hepatitis C virus, hypothyroid, chronic hepatitis C

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INTRODUCTION

A global health issue is hepatitis C occurs due to the (HCV) hepatitis C virus. 3 to 4 million people are newly infected with HCV per year. The World Health Organization, estimated and presented the fact that there are around 180 million HCV patients in the world.¹ In case of chronic HCV, which causes extrahepatic disorders, including hypothyroidism, in addition to hepatic complications.² Some studies have shown that the hepatitis C virus and the autoimmune thyroid are basically liver thyroid diseases. The far more common thyroid disorder noted in patients with HCV infection is Hashimoto's thyroiditis (HT). In chronic hepatitis C (CHC) patients, IFN-alpha therapy is associated with the development of thyroid dysfunction, typically revealing preexisting subclinical

thyroid problems.⁴

Shen Y et al. reported a study involving 1735 HCV infected patients and 1868 Non HCV infected patients pooled Anti-thyroid antibody prevalence tended to be higher in HCV infected subjects and the Hypothyroidism prevalence by HCV was reported 3.10 (95% CI: 2.19-4.40) in HCV infected subjects.⁵

In Pakistan local study reported by Shafiq M I et al. that thyroid dysfunction in upto 27% of HCV positive patients.⁶ Batol N et al. reported a study among 557 ELISA positive HCV patients 9.0% were Hypothyroidism.⁷

Only few studies are available on frequency of Hypothyroidism in patients with HCV infection in Pakistani population. The aim of the study is to determine the frequency of hypothyroidism in HCV infected patients, which may help the future researchers for the early detection and treatment of the disease.

Operational Definitions

Hypothyroidism: was labeled as positive when TSH level is > 4.0 mIU/l and Free T4 < 11.0 pmol/l.

Hepatitis C Infection: Patients with hepatitis C infection having positive serology of anti HCV antibodies were confirmed by ELISA method.

MATERIALS AND METHODS

This cross sectional study was conducted at the department of Gastroenterology, Liaquat National

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Hospital, Karachi. Duration for this research was six months (from 19th Oct 2018 to 19th April 2019). One hundred patients were required to achieve objective of research. Sample size calculated on the basis of the prevalence of Hypothyroidism in patients with Hepatitis C infection $27\% \pm 6\%$ = confidence level= 95%, Absolute 8% precision was required; therefore, sample size was calculated to be 97. Non probability consecutive sampling technique was utilized for the data collection. Patients of either gender between the age of 16-50 years with Hepatitis C infection as per operational definition (for >6 months) and who were not on any treatment for HCV were included in the research. Thyroid patients already taking medications and having treatments or had gone through surgeries, even those who are diagnosed were excluded. Similarly Hepatitis C infected patient previously treated was also excluded. Other co-morbid conditions such as heart failure, renal failure, malnutrition, malabsorption was excluded (because all are effect modifier and can produce bias in my study).

Patients were selected from Gastroenterology Out-Patient Department (OPD), Liaquat National Hospital, Karachi. An informed consent was obtained from patients for including them in study and using their data in research. Based on history, examination and previous-investigations, patients were evaluated for inclusion and exclusion criteria.

History was taken for Hepatitis C infection and a request was sent attached with performa for serum Anti- HCV antibodies by ELISA method and serum Thyroid Stimulating Hormone (TSH), free T4 (FT4) was determined by radio-immune assay technique in the institutional laboratory. Hypothyroidism was considered if TSH is greater than 4.0 mIU/l and FT4 less than 11.0 pmol/l. This information and data regarding age and sex was entered in the performa (attached as annexure) by the principal investigator. During clinical examination of the patients, patients comfort was taken care of. In order to control the bias, exclusion criteria were followed by principal investigator strictly and the investigations were done through the institutional laboratory.

Data was analyzed on SPSS version 22. Mean and standard deviation was calculated for age & duration of HCV. Male and female ratio was calculated. Frequency and percentage was calculated for patients having Hypothyroidism. Data was stratified in different age groups, gender and duration of HCV to control effect modifiers. Post stratification chi-square test was applied by taking $P < 0.05$ as significant.

RESULTS

A total of 97 patients with Hepatitis C infection were selected to conduct this study. The mean age of 33.96 ± 7.247 years. The distribution of age is presented

in Fig.1. The descriptive statistics of age is presented in Table-1.

46 patients (47.4%) were males & 51 patients (52.6%) were females (as shown in Table-2). The mean duration of HCV was 18.21 ± 11.682 months. The distribution of duration of HCV is presented in Graph-2. The descriptive statistics of duration of HCV is presented in Table-1. In our study hypothyroidism was seen in 25 patients (25.8%), as shown in Table-3 The frequencies of age groups, gender, duration of HCV was calculated according to hypothyroidism. The results are presented in Table-4, Table-5 & Table-6 respectively. In our study hypothyroidism in HCV infected patients was more common in age group of 35-50 years, predominant in female gender, was more common in patients with duration of 7-24 months of HCV.

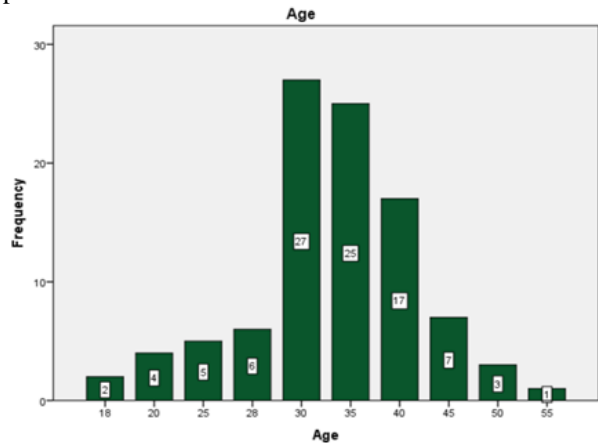


Figure No.1: Frequency distribution of Age (years)

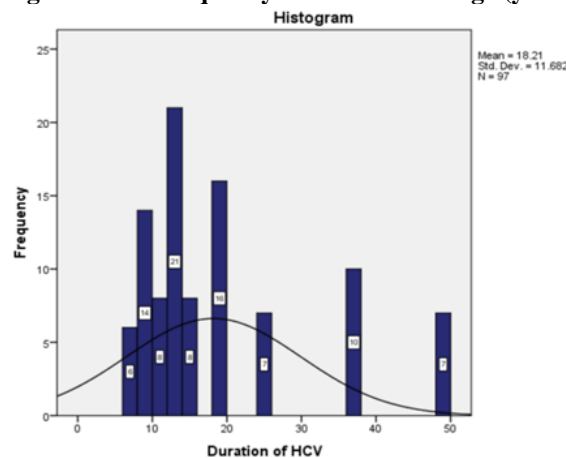


Figure No.2: Frequency distribution of duration of HCV (months)

Table No.1: Descriptive statistics of age, Duration of hepatitis C virus (HCV)

| Statistics | Age (years) | Duration of HCV (months) |
|------------------|-----------------|--------------------------|
| Minimum | 18 | 7 |
| Maximum | 55 | 48 |
| Mean + Std. Dev. | $33.96 + 7.247$ | $18.21 + 11.682$ |

Table No.2: Frequency distribution of Gender

| Gender | N(%) |
|--------|------------|
| Male | 46 (47.4%) |
| Female | 51 (52.6%) |
| Total | 97 (100%) |

Table No.3: Frequency distribution of Hypothyroidism

| Hypothyroidism | n (%) |
|----------------|------------|
| Yes | 25 (28.5%) |
| No | 72 (74.2%) |
| Total | 97 (100%) |

Table No.4: Hypothyroidism According to Age

| Age | Hypothyroidism | | Total | P-Value |
|-------------|----------------|------------|------------|---------|
| | Yes | No | | |
| 16-34 years | 8(8.24%) | 36(37.11%) | 44(45.36%) | 0.293 |
| 35-50 Years | 17(17.52%) | 36(37.11%) | 53(54.63%) | |
| Total | 17(17.52%) | 72(74.2%) | 97(100%) | |

Table 5: Hypothyroidism According to Gender

| Gender | Hypothyroidism | | Total | P-Value |
|--------|----------------|-----------|------------|---------|
| | Yes | No | | |
| Male | 9(9.3%) | 37(38.1%) | 46(47.42%) | 0.184 |
| Female | 16(16.5%) | 35(36.1%) | 51(52.57%) | |
| Total | 25(25.8%) | 72(74.2%) | 97(100%) | |

Table No.6: Hypothyroidism according to duration of hepatitis C virus (HCV)

| Duration of HCV | Hypothyroidism | | Total | P-Value |
|-----------------|----------------|-------------|-------------|---------|
| | Yes | No | | |
| 7-24 Months | 19 (19.58%) | 61 (62.88%) | 80 (82.47%) | 0.021 |
| 25-48 Months | 6 (6.18%) | 11 (11.34%) | 17 (17.52%) | |
| Total | 25 (25.8%) | 72 (74.2%) | 97 (100%) | |

DISCUSSION

The goal of this research was to determine the prevalence of thyroid dysfunction in patients with HCV infection who visited the Liaquat National Hospital, Karachi. As compared to the Batool et al⁸ study in which improper thyroid functioning was observed at the rate of 15.2 percent HCV patients. Our findings presented that thyroid dysfunctioning is figured in almost 25.8 percent of the patients. The above figure is consistent with research performed in other states showing thyroid improper functioning in 7% -15% of patients which are untreated with HCV 2-5. In interferon-free HCV patients, a recent study of such studies recorded a 10-15 percent incidence of TD^{14,8}. Our prior outcome of an eminent incidence of TPO-Ab i.e., (26.8 percent) in patients who confirms high incidence of TD⁹. Local studies have identified a prevalence of TD ranging (7% to 22%) in patients of HCV prior to interferon therapy in other cities in Pakistan.¹⁰⁻¹³

In the general population, the occurrence of TD is approximately 5 percent, with a higher rate of hypothyroidism than hyperthyroidism^{14,15}. According to our findings, while the overall prevalence of TD was far much higher than in the common people, in HCV patients there was a trend of comparatively more hypothyroidism (9.0 percent) than hyperthyroidism (6.3 percent). This finding is consistent with other studies that have reported a higher incidence of hypothyroidism relative to hyperthyroidism in patients with HCV¹⁴⁻¹⁶. According to the new meta-analysis, the patients of HCV were three times more vulnerable than control subjects to hypothyroidism¹⁷. Taking into account the high occurrence of TPO-Ab in patients with HCV (local), anticipated that this hypothyroidism is likely to be autoimmune¹⁵. Confirmation, however, is important since HCV infection is also documented in non-autoimmune hypothyroidism.¹⁸.

Several devices for the stimulation of autoimmune thyroiditis through HCV have been suggested in various studies, such as molecular impression among viral antigens and self-antigens, stimulation of (bystander mechanism) autoreactive T cells through local infection induction, induction of peculiar expression on thyroid cells of MHC, (class II molecules), viral changes stimulation in self-antigen appearance. The HCV that induces thyroid autoimmunity in a predisposed person, on the other hand, is still mysterious. Two theories, i.e. molecular simulation and an observer activation, provide the authentic evidence of the production of thyroid autoimmunity in patients already having hepatitis C virus among the above-mentioned mechanisms. The theory of molecular mimicry proposed that a similar classification of nucleotides among self-proteins and the viral proteins may induce a cross-over immune reaction to self-antigens counterfeit by proteins of "infectious agents"²⁰⁻²¹

Although HCV was unable to spread a virus to thyroid cells, the other parts of the body were also infected by a virus coat that is essentially a protein; a major physiological effects. For example, 2 proteins (structural) of HCV, i.e. E1 and E2, are able to bind to certain molecules of the body surface, i.e. CD81, which assist in viral entry²¹. Local inflammation caused by viral infection according to the bystander activation hypothesis; as an outcome, stimulation occurs of autoreactive T lymphocytes that have been repressed by peripheral tolerance mechanisms by Treg cells (regulatory T cells) ²¹. The bystander activation mechanism is supported by recent facts as the main process through which hepatitis C infection induces autoimmune thyroiditis. Therefore, the association between thyroid autoimmunity and hepatitis C virus infection has been shown to be triggered by thyroid HCV infection as a result of the release of pro inflammatory mediators, such as IL-8, and the

production of thyroid autoimmunity via the bystander activation phase⁹.

Due to the high occurrence of thyroid autoimmunity among females, majority studies have reported a higher threat or occurrence of TD affecting females effecting from HCV equally compare to the male patients 22,23. Female HCV patients in this report had a greater risk and occurrence of TD comparatively from male patients i.e., (16.1% Vs 12.5%), yet the variance was not substantial. The outcome is close to that of a indigenous study¹¹ and confirmed by our prior result of a compatible occurrence of TPO-Ab specifically in patients with HCV in men and women¹⁰. Although other studies also report a non-significant gender gap in the incidence of TD.^{24, 25}. The most likely explanation likely to be the reason of the low number of male patients included in this study (less than one-third female patients). The ratio of TD in them may be decreased towards a substantial level by a growing number of male patients. Even if male patients be more than females, a former Chinese study showed a greater occurrence of TD in female patients.²⁶.

In females, thyroid autoimmunity is improved compared with male subjects¹⁶⁸. Different studies have documented a similar pattern in HCV infected patients.^{26, 27}.

Local studies in Pakistan have testified TD in HCV patients (20%) after treatment with IFN-alpha and ribavirin^{28, 29}. Local studies showed that TD in 20% patients of HCV subsequent treatment with IFN-alpha and ribavirin^{28,29}. This high incidence can be hypothesized to be due to pre-existing in TD patients. The pre-treatment screening is also suggested for every patient effecting from HCV scheduled for IFN-alpha therapy.

CONCLUSION

It is observed that HCV itself induces biochemical thyroid dysfunction in 25.8 % patients prior to treatment.

Author's Contribution:

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|----------------------------|--|
| Concept & Design of Study: | Hafeez Yaqoob |
| Drafting: | Shahid Karim, Muhammad Tanweer Khalid |
| Data Analysis: | Hamid Ali, Afsheen Faryal, Ghulam Mujtaba |
| Revisiting Critically: | Hafeez Yaqoob, Shahid Karim |
| Final Approval of version: | Hafeez Yaqoob |

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