Original Article

Serum Resistin Levels in Non-Diabetic Patients of Hepatitis C in Hazara Division

Alamzeb Jadoon[1], Ayesha Gohier[1], Nazish Butt[2] and Khalid Pervez Lone[1]

ABSTRACT

Objective: Resistin is a 12-Kd protein synthesized and secreted in adipose tissue. It is member of C-terminal cysteine rich protein family. Serum resistin levels increase in chronic inflammatory conditions. In the current study, the levels of serum resistin were estimated in healthy, interferon (IFN) treated and untreated groups of Hepatitis C (HC) to assess its role as inflammatory biomarker. Resistin is said to be affected in diabetes mellitus.

Study Design: Analytical study

Place and Duration of Study: This study was conducted at the Department of Physiology and Cell Biology, University of Health Sciences Lahore from May 2013 to November 2015.

Materials and Methods: 28non-diabetic subjects of both sexes were recruited in each group and compared within the groups (Control, Untreated and Treated HC patients). PCR was done for viral load. Serum resitin was measured by using ELISA.

Results: Mean serum levels of resistin were higher in untreated HC patients as compared to INF treated HC patients but the difference was not significant. However, significant difference was observed among the males and females of untreated HC group in which males had higher values than females.

Conclusion: Serum resistin levels are lower in healthy and INF treated individuals as compared with the untreated subjects or hepatitis C. However, the difference was not significant but similar study with larger sample size is recommended to establish cause effect relationship.

Key Words: Hepatitis C, Interferon, Resistin

Citation of article: Jadoon A, Gohier A, Butt N, Lone KP. Serum Resistin Levels in Non-Diabetic Patients of Hepatitis C in Hazara Division. Med Forum 2021;32(4):76-78.

INTRODUCTION

Hepatitis C (HC) is a chronic disorder caused by a small, enveloped RNA virus of family Flaviviridae and genus Hepacivirus. It affects approximately 170-200millionpeople worldwide and about 350000 people die from its complications [1,2]. Pakistani population has a prevalence rate of about 8-10 per cent that estimated approximately 10 million[3]. It is most common cause of hepatocellular carcinoma. Use of infected needles, transfusion of contaminated blood, intravenous drug abuse, quackery, infected blades at barbar shops are the most common causes of spread if hepatitis C[4].

HC virus hassubtypes (1-6) and more than 50 sub genotypes[5]. Out of these genotypes, 3a is most common along with type 1 a in Pakistan and has got better viral eradication rates in terms of end of treatment response (ETR) and sustained viral response (SVR) after treatment with INF and antiviral Ribavarin[6,7,8,9].

Resistin is a 12-Kd protein synthesized and secreted in adipose tissue. It is member of C-terminal cysteine rich protein family. Serum resistin levels increase in chronic inflammatory condition[10].Human resistin is among the inflammatory regulators of downstream action of macrophages, peripheral blood mononuclear cells (PBMCs) and vascular cells. On stimulation with recombinant human resistin, human macrophage cells, PBMCs, and hepatic stellar cells produce TNF-α, IL-6, IL-12, and MCP-1 through NF-κB-mediated pathway. Resistin works by autocrine, paracrine, and endocrine mode of action and affects vast array of cell types and tissues. Circulatory resistin level has been positively correlated with common inflammatory and fibrinolytic biomarkers such as CRP, TNF-α, and IL-6 in type 2 diabetes, rheumatoid arthritis, chronic kidney disease, sepsis, and coronary atherosclerosis, whereas level of resistin in blood plasma is associated with disease severity in case of sepsis and pancreatitis[11].

HC infection is diagnosed by using ELISA followed by quantitative and qualitative PCR. Quantitative PCR gives an estimated viral load or number of viruses in the blood of the affected person. IFN treated patient should ideally have undetected viral load at the end of treatment. ETR is the amount of viral load at the end of

[1.] Department of Physiology / Biochemistry[2], University of Health Sciences, Lahore.

Correspondence: Ayesha Gohier, M.Phil Scholar, Physiology Department, University of Health Sciences, Lahore.
Contact No: 0331-4300567
Email: ayeshagohier@hotmail.com

Received: June, 2020
Accepted: January, 2021
Printed: April, 2021

treatment and SVR is the viral load 24 weeks after treatment[12]. ETR and SVR are reliable tools that can be used for the success of IFN treatment in any HC patient and disease prognosis[9].

Nearly 75-80 per cent of the HC infections end up into chronic stage and only 20-25 percent are spontaneously resolve with or without treatment in the acute stage[13].

Progression of HC to chronic stage may be due to persistent inflammation superadded by increased serum resistin levels in infections as in untreated hepatitis C. Resistin prolongs inflammation by production of pro-inflammatory cytokines as well as increasing cell adhesion molecules for chemotaxis process. Resistin is increased in Diabetic and obese patients[14].

MATERIALS AND METHODS

The current study included a total of 84 adult non-diabetic subjects (28 each group) from Hazara division of Khyber Pakhtunkha province including both genders equally. The study was approved by the Ethical Committee and Research Board of the University of Health Science, Lahore and DHQ Hazara division.

Group I:28 adults age 18-60 years without any apparent disease or viral infection.

Group II: untreated, fresh cases of HCV diagnosed by ELISA/PCR age 18-60 years.

Group III: Treated HCV patients with age 18-60 years who completed INF therapy last week.

Subjects having diabetics, hepatitis A, hepatitis B, any acute or chronic infection and obesity BMI >25 were excluded from the study. The subjects included in the study were examined in detail and were screened for exclusion criteria. A detailed history was taken from all the participants about the prior knowledge of disease, possible source of infection and screening status of their families.

Study Design: This is an analytical comparative study.

Blood Collection: After 10- 12 hours of overnight fast, 5 ml of blood was drawn from the superficial vein by aseptic techniques. Fasting blood glucose was checked by a glucometer (Xceed, Abbott). Blood was secured in SST vacutainers (yellow top) for extraction of serum. Serum was extracted by centrifuging the blood for 10 minutes at 3000 rpm. The serum was stored at – 80°C in Eppendorf still further analyzed. Serum resistin levels were measured using commercially available ELISA kits (Glory Science Co., USA). PCR was done for viral load estimation.

Statistical Analysis: The data were entered and analyzed using IBM S.P.S.S.(Statistical Package for Social Sciences software for windows) version 20. Mean ± SD was given for quantitative variables (age, serum resistin levels). Frequencies and percentages were given for qualitative variables (gender, sample group).

Shapiro-Wilk test was used to test the normality of data. The data given either as mean± SD for normally distributed variables or median IQR for non-normally distributed variables. The variables were compared to see any significant difference in their means. In case of normally distributed data, single factor ANOVA was applied followed by Tukey's post hoc test for three groups. Independent "t" Test was used for comparing means of parametric data.

RESULTS

Mean± SD of serumresistin levels of controls, untreated and treated groups were 4.32±0.99,5.33±2.32 and 4.69±2.32 respectively whereas Median (IQR) values were 3.95(3.35-6.87) for controls, 4.20 (3.01 -15.78) for untreated and 3.83 (2.81-13.40) for treated showed no significant difference (Kruskal-Wallis test; p =0.446).

Comparison of resistin between Treated & Untreated: No significant difference in resistin levels was found in treated and untreated group (Mann-Whitney U Test; p = 0.249).

Comparison of resistin between Controls &Treated No significant difference was found in controls and treated patients (Mann-Whitney U Test; p= 0.476).

Comparison of resistin between Controls & Untreated: No significant difference was found in levels of resistin in controls and untreated cases (Mann-Whitney U Test; p= 0.431).

DISCUSSION

Mean resistin levels in treated group (4.69 ug/L) and untreated group (5.33 ug/L) of HC cases were found to be higher than control group (4.32 ug/L) however, this difference was not significant (p=0.446). The only Significant difference for resistin levels was observed in untreated male and females (Mann Whitney test; p=0.046). study conducted by Iaconoin 2007 found that resistinlevels do not change during and after treatment[15]. Although mean serum resistin level of untreated HCV cases was higher (5.33 ug/L), than control value (4.23 ug/L) and treated cases (4.20 ug/L) but this difference was found to be statistically insignificant (p= 0.446). A study by Morace et al. also reported higher levels of resistin in HCV patients as compared to controls[16]. Normal serum levels of resistin were 5.3 (ng/mL) in controls and 12.1 (ng/mL) in HCV cases according to Tifticki et al in 2009[17].

Resistin is an adipocytokine secreted by adipose tissues so body fat content can affect serum levels of resistin as seen in studies by Azuma et al., in 2003, whereby subjects having body mass index (BMI) of more than 31 had higher mean (±SD) serum resistin levels (12.83±8.30)[18]. Similarly, a study by Zaidi and Shirwanyin 2015 also reported higher mean (±SD) (25±5) serum resistin levels in subjects havingBMI of more than 33[19]. In another study published in 2016, Niaz and Shirwany reported mean (±SD) serum resistin levels of 6.8 ±1.01 however BMI was not mentioned[20]. Our values of resistin, therefore, seem similar to the

values reported by other authors for lean subjects. Also, any difference reported here can be because of ethnic differences as our samples were collected from Hazara division (Abbottabad/Mansehra) which comes in Khyber PakhtunKha province while the subjects of Niaz and Sherwany were from Punjab province (Lahore).

CONCLUSION

A significant difference was found in serum resistin levels among male and females of untreated group. The difference in gender may be due to difference in fat distribution and percentage between the genders. The levels of resistin were lower in interferon treated cases of HC as compared to untreated cases. May be a study with higher number of samples and with a small age range between the sample population would have given significant difference between all groups.

Author's Contribution:

Concept & Design of Study:	Alamzeb Jadoon
Drafting:	Ayesha Gohier, Nazish Butt
Data Analysis:	Khalid Pervez Lone
Revisiting Critically:	Alamzeb Jadoon, Ayesha Gohier
Final Approval of version:	Alamzeb Jadoon

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Choo QL, KuoG, Weiner AJ, Overby LR, Bradley DW, Houghton M. Isolation of a cDNA clone derived from a blood-borne non-A, non-B viral hepatitis genome. Science 1989; 244: 359–62.
2. Averhoff FM, Glass N, Holtzman D. Global burden of hepatitis C: considerations for healthcare providers in the United States. Clinical Infect Dis 2012;55(suppl_1):S10-5.
3. Butt S, Idress M, Akbar H, Rehman I, Awan Z, Afzal S, et al. The changing epidemiology pattern and frequency distribution of hepatitis C virus in Pakistn. Infection Genetics and Evolution 2010;10(5):595-600.
4. Manns MP, Buti M, Gane ED, Pawlotsky JM, Razavi H, Terrault N, et al. Hepatitis C virus infection. Nature Reviews Disease Primers 2017;3(1):1-9.
5. Grebely J, Dore GJ, Alami NN, Conway B, Dillon JF, Gschwantler M, et al. Safety and efficacy of glecaprevir/pibrentasvir in patients with chronic hepatitis C genotypes 1–6 receiving opioid substitution therapy. Int J Drug Policy 2019;66: 73-9.
6. RehmanI, Idrees M, Ali M, Ali L, Butt S, Hussain A, Akbar H, Afzal S. Hepatitis C virus genotype 3a with phylogenetically distinct origin is circulating in Pakistan. Genet Vac Ther 2011;9:2.
7. Ali A, Nisar M, Ahmad H, Saif N, Idrees M, Bajwa MA. Determination of HCV genotypes and viral loads in chronic HCV infected patients of Hazara Pakistan. Virol J 2011;8:466.
8. Attaullah S, Khan S, Ali I. Hepatitis C virus genotypes in Pakistan: a systemic review. Virology 2011;8:433.
9. Amir M, Rahman AS, Jamal Q, Siddiqui MA. End treatment response and sustained viral response in hepatitis C virus genotype 3 among Pakistani population. Annals Saudi Med 2013;33(6):555-8.
10. Kastin A, editor. Handbook of biologically active peptides. Academic press;2013.
11. Tripathi D, Kant S, Pandey S, Ehtesham NZ. Resistin in metabolism, inflammation, and disease. The FEBS J 2020;287(15):3141-9.
12. Rosen HR. Chronic Hepatitis C Infection. N Eng l J Med 2011;364:2429-38.
13. Holmes J, Thompson A, Bell S. Hepatitis C: an update. Australian J General Pract 2013;42(7):452.
14. El-Miligy D, Mohammed Z, Atta MM, Belal TH, Mahran YZ. Study of Serum Resistin Levels in Patients with Chronic Hepatitis C Viral Infection. Scientific J Uni 2014;2(1):12-7.
15. Lo Iacono O, Venezia G, Petta S, Mineo C, De Lisi S, Di Marco V, et al. The impact of insulin resistance, serum adipocytokines and visceral obesity on steatosis and fibrosis in patients with chronic hepatitis C. Alimentary Pharmacology Therapeutics 2007;25(10):1181-91.
16. Morace C, Spadaro A, Cucunato M, Tortorella V, Consolo P, Luigiano C, et al. High serum resistin in chronic viral hepatitis is not a marker of metabolic disorder. Hepatogastroenterol 2010; 57(102-103):1215-9.
17. Tiftikci A, Atug O, Yilmaz Y, Eren F, Ozdemir FT, Yapali S, et al. Serum Levels of Adipokines in Patients with Chronic HCV Infection: Relationship with Steatosis and Fibrosis. Arch Med Res 2009;40:294-298.
18. Azuma K, Katsukawa F, Oguchi S, Murata M, Yamazaki H, Shimada A, et al. Correlation between serum resistin level and adiposity in obese individuals. Obes Res 2003;11(8):997-1001.
19. Zaidi SI, Shirwany TA. Relationship of serum resistin with insulin resistance and obesity. J Ayub Med Coll Abbottabad 2015;27(3):552-5.
20. Niaz S, Shirwany TAK. Serum Resistin Levels in Patients of Hypertension and Coronary Artery Disease. PJMHS 2016;10(2):445-447.