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Research Article

**A RANDOMISED CONTROL TRIAL TO COMPARE THYROID
DISORDER (TD) AMONG CHC (CHRONIC HEPATITIS C)
PATIENTS: IFN- α Vs PEG-IFN THERAPY**¹Dr. Razwan Siddeq, ¹Dr. Shahid Mehmood, ²Dr. Muhammad Umair Abid¹Jinnah Hospital Lahore²Mayo Hospital Lahore**Abstract:**

Objectives: The research objective is to find out the rate of thyroid disorders among patients with chronic hepatitis C when they treated with pegylated interferon comparing to the treatment through interferon alpha.

Materials & Methods: The research method is randomised Controlled Trial, which was carried out at Allied Hospital, Faisalabad from September 2016 to August 2017. Subject size of 340 patients with Chronic Hepatitis C (CHC) selected by PSR HCV RNA. Patients were of both genders, having 25 – 60 years age range.

Results: Subjects were divided into Group – A and B. Mean age of Group – A was (35.7 \pm 07.3) years and Group – B was (35.9 \pm 08.2) years. Male and female patients were 59.1% (201) and 40.8% (139) with (2.0:1) ratio. The mean level of thyroid-stimulated hormone in Group – A and B was (02.3 \pm 1.1) and (02.4 \pm 0.9) respectively. Thyroid disorder found in conventional and pegylated IT was found among 08.82% (15) and 18.2% (31) patients with p-value = 0.011.

Conclusion: The study concludes that when patients with CHC treated with interferon alpha, a lower frequency of thyroid disorder found compared to the treatment of pegylated interferon. This frequency is higher among females of both groups.

Keywords: Chronic Hepatitis C (CHC), Interferon Alpha (IA), Pegylated Interferon (PI), Interferon Therapy (IT), Thyroid Disorder (TD) and Thyroid Stimulating Hormone (TSH).

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INTRODUCTION:

The virus of hepatitis C comes from the Flaviviridae family. A single-stranded RNA genome (Positive) makes HCV virion [1]. The presence of RNA in a hepatitis C virus, which persists for more than six months, called a CHC [2]. CHC is present among 150 million people approximately. Egypt has the highest prevalence of 15 to 20%, while the lowest prevalence of 0.01 to 0.1% is present in the United Kingdom [3]. The prevalence of CHC in Pakistan is at the worst level of 4.8% of its population [4, 5]. Hepatitis C spreads from using unsterilized, sharp instruments, blood/blood products transfusion, and tattoos [5]. The mainstay of the treatment of hepatitis C is the combined therapy of ribavirin and interferon [2]. Treatment through interferon antiviral therapy comes with the side effect of thyroid dysfunction where we may reduce the dose or discontinue therapy [6]. Contrary to developed countries, Pakistan still uses conventional interferon because of its being cost-effective [6]. The development rate of TD is based on the type of treatment (pegylated vs. conventional interferon) and population. A local study shows 18.69% (20/107) development of TD using conventional interferon treatment [7]. Another study showed this rate to be 18% (18/100) [8]. These results are different regarding population. For example, a French population shows a 10% rate of TD [9]. No local study exists on PI therapy. However, a study shows greater TD rate (14% vs. 6%) in PI than conventional interferon (p-value=0.0029) [10]. Our study aims at comparing the frequency of thyroid disorder among patients of CHC when they are being treated through IA versus PI in our population. The population of the subcontinent has a different diet, environment, the rate of development of thyroid disorder, and genotype as described earlier. The same way, PI may produce different TD rate, which this study intended to find. PI is costly but they have the advantage of convenient dosing and better efficacy. Our study intends to produce evidence-based results regarding TD while using interferon treatments so that it helps physicians in choosing a better option of treatment in the context of Pakistan. To fulfil this purpose, we planned a comparative treatment between IA and PI in the prevention of TD among CHC patients.

MATERIAL AND METHODS:

The research method is randomised Controlled Trial, which was carried out at Allied Hospital, Faisalabad from September 2016 to August 2017. We enrolled patients of CHC (Diagnosed by PSR HCV RNA), both gender, age 25 – 60 years, THS level as Normal (0.4 to 4 mU/L) and six-month duration of interferon therapy. Whereas, we did not include the patients with a history of earlier TD treatment, patients

determined with ascites, cirrhosis, and splenomegaly (chronic liver disease) through lab examination, history of earlier interferon treatment and patients determined with connective tissue disorder (Rheumatoid arthritis, SLE).

With informed written consent from each patient fulfilling criteria of inclusion and approval from an ethical committee of the hospital, a subject size of 340 patients was selected. Patients were divided into Group – A (conventional interferon therapy) and Group – B (PI) randomly. The outcome of TD was measured six months after the therapy of interferon. Thyroid disorders: TD was defined as Hypothyroidism with a level of TSH serum > 4.0mU/l or <0.4mU/l.

Each patient's demographic data and a pre-therapy thyroid function test were recorded on a predesigned Performa. Data analyzation was carried out using SPSS. Level of TSH and age were presented as SD and mean. The presence of TD and gender were taken for frequency. The comparison of the frequency of TD in Group-A and B was done through Chi-Square with p-value ≤ 0.050 considered as significant. With a p-value of ≤ 0.050 considered as significant, gender, age stratification was done, and the Chi-square test (Post-stratification) was applied.

RESULTS:

Subject size of 340 patients having a mean age of (35.8 \pm 07.8) years was selected for this study. Mean age of Group – A and B was (35.7 \pm 07.3) and (35.9 \pm 08.2) years respectively. Patients 32.3% (110) of the age group 25 – 35 year were in majority (Table – I). A number of male and female patients was 59.1% (201) and 40.8% (139) respectively (Table – II). Mean level of TSH in Group – A and Group – B was (02.3 \pm 01.1) and (2.4 \pm 0.98) respectively. The rate of TD among the patients of Group – A and Group – B was 08.8% (15) and 18.2% (31) respectively, having p-value = 0.011 (Table – III). Patients' stratification with the reference of gender and age was carried out. For the age group of 25 to 35 years, TD was recorded among 12.9% (07) and 19.6% (11) patients of Group – A and B respectively, with p-value = 0.3440 as insignificant. TD was recorded 8.16% (04) and 16% (08) patients of Group – A and B respectively, for the age group of 36 – 45 years, with p-value = 0.2320 as insignificant. The development of TD among the patients of 46 to 55 age group was 04.88% (02) and 11.9% (05) in Group – A and B with an insignificant difference of p-value 0.249. A significant difference of TD with p-value = 0.033 was found among 56 to 60 years age group (Table – III). The frequency of TD among male and

female was found 90% (91) and 81% (81) for Group – A and 92.7% (64) and 82.8% (58) for Group – B, with the insignificant difference of p-value = 0.066 and p-value= 0.075 respectively (Table – IV).

Table-I: Group – A and B; Distribution of age

Age (Years)	Group - A (170)		Group - B (170)		Total (340)	
	Number	Percentage	Number	Percentage	Number	Percentage
25 - 35	54	31.76	56	32.94	110	32.35
36 - 45	49	28.82	50	29.41	99	29.12
46 - 55	41	24.12	42	24.71	83	24.41
56 - 60	26	15.29	22	12.94	48	14.12
Mean \pm SD	35.73	7.31	35.91	8.24	35.79	7.86

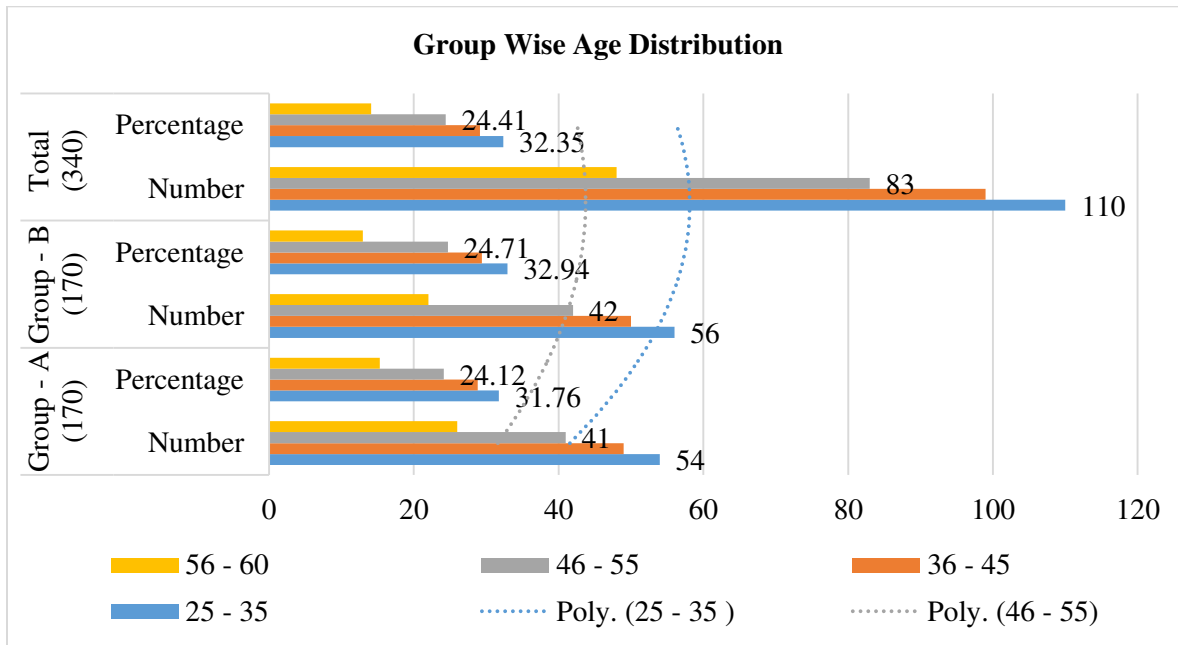


Table – II: Distribution according to gender

Gender	Number	Percentage
Male	201	59.12
Female	139	40.88

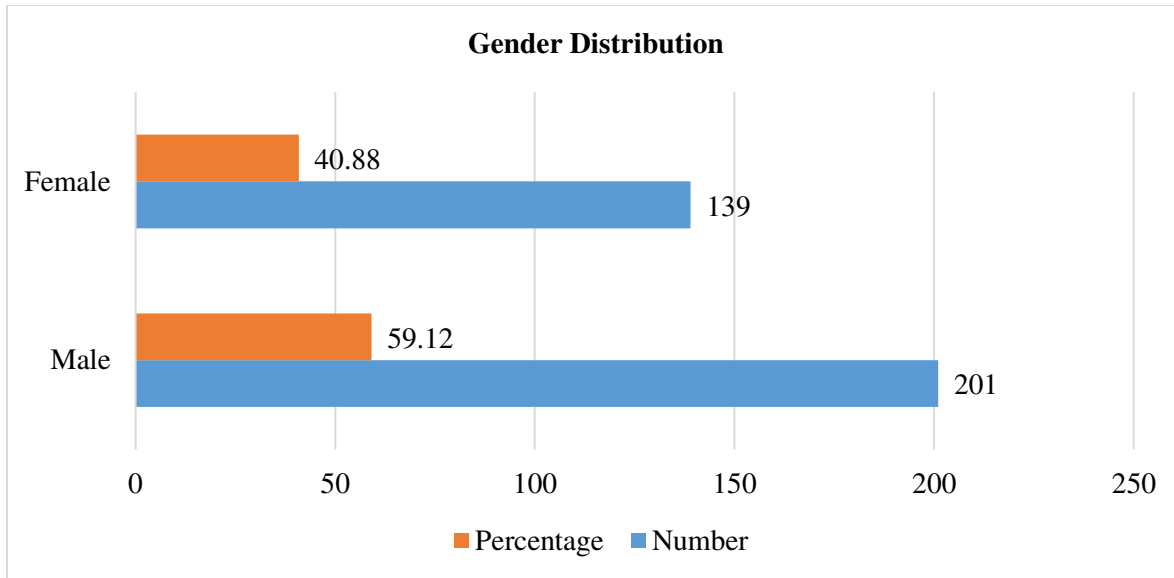


Table – III: Frequency of Thyroid Disorder in both groups

Patient's Frequency	Group - A		Group - B	
	Number	Percentage	Number	Percentage
Present	15	8.82	31	18.24
Absent	155	91.18	139	81.76

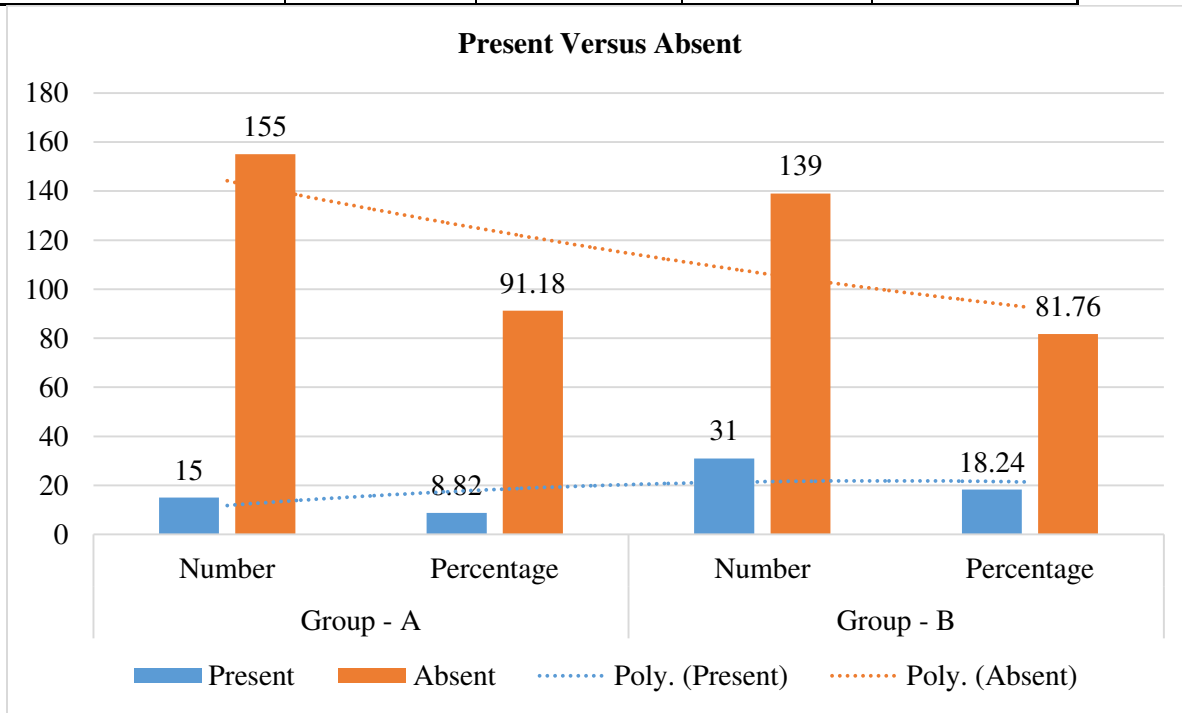
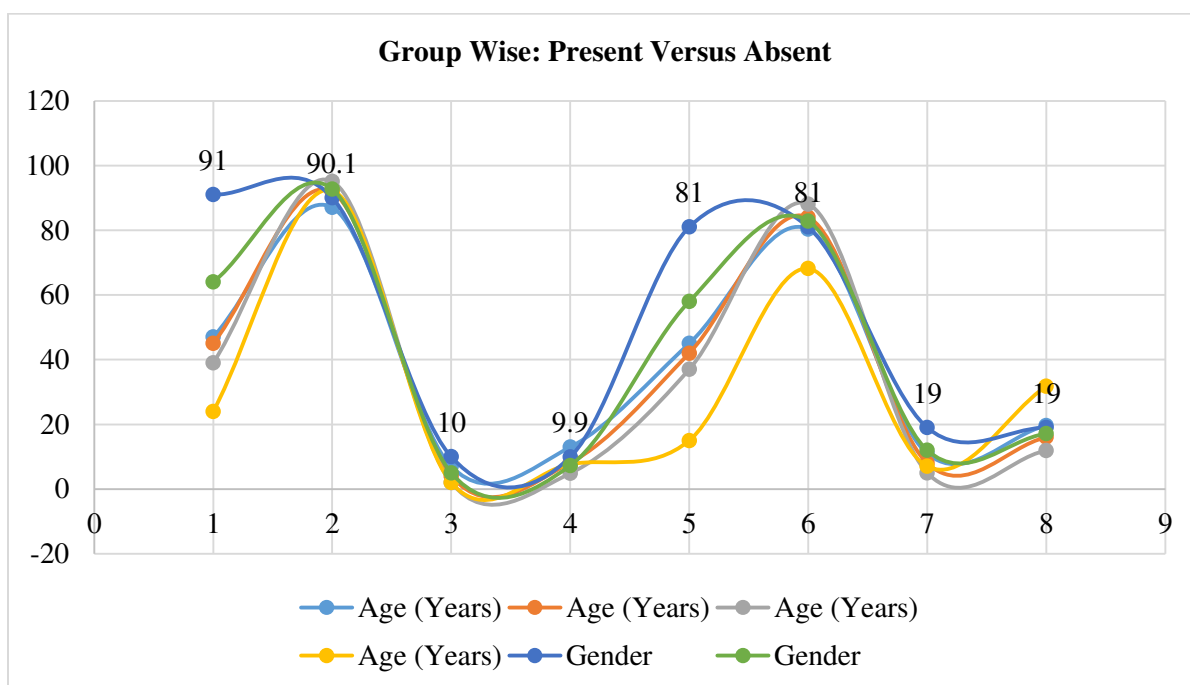


Table – IV: Age and Gender Stratification

Variables		Group - A (170)				Group - B (170)				P-Value
		Absent		Present		Absent		Present		
		No	%	No	%	No	%	No	%	
Age (Years)	25 - 35	47	87.04	7	12.96	45	80.36	11	19.64	0.344
	36 - 45	45	91.84	4	8.16	42	84	8	16	0.232
	46 - 55	39	95.12	2	4.88	37	88.1	5	11.9	0.249
	56 - 60	24	92.31	2	7.69	15	68.18	7	31.82	0.033
Gender	Male	91	90.1	10	9.9	81	81	19	19	0.066
	Female	64	92.75	5	7.25	58	82.86	12	17.14	0.075



DISCUSSION:

WHO shows 180 million cases with 350 thousand mortalities per year around the world due to hepatitis C infection [11]. To manage HCV, FDA approved 02 telaprevir, protease inhibitors, and boceprevir (1st generation). Peg-IFN and Ribavirin are still the major elements of the treatment but TD is its one of the major side effects [12]. The mechanisms of the prevalence of TD during interferon treatment remain unclear [13]. The IFN- α projects inhibitory effect on the metabolism, release and synthesis of thyroid hormones. In addition, major histocompatibility antigens affect thyroid cells due to abnormal expression [14]. Our study is a comparison of using peg-IFN or IFN- α for the treatment of TD in the dealing of CHC. In this study, the (35.8 \pm 07.8) year was the average age. The average age in Group – A and B was (35.73 \pm 07.31) and (35.9 \pm 08.24) years

respectively with 32.3% (110) of the cases from 25 – 35 years age group. The outcomes of this study are similar to Aziz S et al and lower to Yan Z et al with average/mean age of thirty-three and forty years respectively [15, 16]. A much lower mean age of twenty-seven years was found in Othmane BM et al study as compare to our study [17]. We took 340 patients where male and female patients were 59.1% (201) and 40.8% (139) with (2.0:1) ratio. A huge number of male subjects has been found in previous studies as well [15, 16]. The rate of TD among the patients of Group – A and B was 08.8% and 18.2% respectively, having p-value = 0.011. Yan Z et al used IFN- α , IFN- α + Ribavirin, peg-IFN- α + Ribavirin in his study which developed a TD rate of 8%, 8.6%, and 13.80% respectively with the p-value= 0.145 recorded as insignificant. The outcomes of Kee KM et al study also shows an insignificant p-value of

1.000 between TD frequency using Peg-IFN and Standard IFN treatment [16 – 18]. Two local studies show 18.69% (20/107) and 18% (18/100) development of TD using conventional interferon treatment [7, 8]. Both studies have a difference in outcomes comparing to other population, as the French population has TD frequency of 10% [9]. The study concludes that TD has a higher frequency with PI treatment (14.1%) comparing to conventional interferon treatment (6%) (P-value 0.0029) [10]. The outcome of a study was 2% to 3% TD using interferon alpha treatment [19]. Two more studies show TD frequency of 15% and 21% with IFN- α and Peg-IFN treated cases [20, 21].

CONCLUSION:

This study concludes that the patients of CHC present lower frequency of TD when they are being treated with interferon alpha as compared to the treatment with PI in the population of Pakistan. Female gender has a higher rate of TD in both groups. Therefore, it is recommended to use interferon alpha as the first choice to prevent thyroid disorder among patients of chronic hepatitis C. This will also help in the reduction of morbidity among CHC patients.

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