RATE OF INFLUENZA VACCINATION AMONG PATIENTS OF RHEUMATOID ARTHRITIS RECEIVING IMMUNOSUPPRESSIVE DRUGS IN ISLAMABAD.

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ABSTRACT... Objectives: The aim of our study was to assess the rates of influenza vaccinations in patients of rheumatoid arthritis receiving immunosuppressive drugs in a tertiary care hospital in Islamabad. Study Design: Cross-sectional study. Setting: Medical outpatient unit of the HBS General Hospital, Islamabad. Period: From October 2018 to January 2019. Material & Methods: Included 108 patients of rheumatoid arthritis selected through nonprobability purposive sampling and Patients with at least one year history of Rheumatoid arthritis currently receiving immunosuppressive therapy were included in the study. Socio-demographic details and vaccination history was collected on a pre-designed performa. Data was analyzed using SPSS version 23. Chi square test was applied to ascertain association. Results: Out of the total 108 patients, 80 were females and 28 were males. Average duration of RA among the study sample was 4.6 years. 34% of the patients reported having co-morbid medical condition(s). Only 3% of the patients had received influenza vaccination. 22% of the patients reported severe influenza infection during the preceding season. Lack of awareness about the importance of vaccination was the main reason for low vaccination rate. Conclusion: The rates of influenza vaccination in patients of rheumatoid arthritis receiving immunosuppressive drugs are extremely low in Islamabad. There is an urgent need to raise awareness on this issue among the patients as well as physicians.

Key words: Rheumatoid Arthritis, Influenza, Vaccination.

INTRODUCTION
Influenza is a common, highly contagious viral infection which affects the respiratory system. Globally, 5–10% of adults and 20–30% of children are affected by influenza annually.¹ In Pakistan the rates of influenza infection have shown a gradual and persistent increase since 2009.² In most cases influenza is a self-limiting disease with mild symptoms. However, in vulnerable patients it can lead to significant morbidity.³ WHO recommends annual influenza vaccination as the most efficient method of prevention of infection and its complications.¹

Patients with chronic illnesses such as rheumatoid arthritis are at an increased risk of infections.³ A retrospective longitudinal cohort study by Doran et al. on 609 rheumatoid arthritis patients showed infection rate was 70–80 % higher in these subjects than the general population.⁴ Rheumatoid arthritis patients are also more likely to develop serious complications with influenza infection. This increased likelihood is partly due to the disease itself and partly due to treatment with disease modifying immunosuppressive agents.⁵ International organizations such as British Society for Rheumatology and European League against Rheumatism (EULAR) recommend influenza vaccination annually in patients with rheumatoid arthritis who are on treatment with disease modifying anti-rheumatic drugs (DMARDs).⁶,⁷

Despite these international recommendations, studies conducted in different countries of the world have observed a low prevalence of influenza vaccination among rheumatoid arthritis patients.⁸-¹⁰ A study conducted by Hmamouchi et al on 3920 rheumatoid arthritis patients enrolled
across 17 countries reported an overall rate of 25.3% for influenza vaccination and huge disparity between countries (less than 1% in Morocco and Egypt – 66.2% in Japan).11 To our knowledge, there is no data available about awareness and the rates of influenza vaccination in rheumatoid arthritis patients in Pakistan. The aim of our study was to assess the rates of influenza vaccination in patients of rheumatoid arthritis receiving immunosuppressive therapy in a tertiary care hospital in Islamabad.

MATERIAL AND METHODS
This descriptive cross-sectional study was conducted from October 2018 to January 2019 at the medical outpatient department of HBS General Hospital, Islamabad.

Patient presenting to the OPD with history of rheumatoid arthritis for more than one year and receiving immunosuppressive drugs were approached for the study.

108 patients of rheumatoid arthritis were included in the study using non-probability consecutive sampling technique.

Ethical approval for the study was obtained from the relevant authority of the hospital. Patients were informed about the aims and the structure of the study. Written informed consent was taken from all patients willing to participate. A self-designed questionnaire was used to collect the information. The data included demographic variables, history of influenza vaccination, patient’s awareness about the need for vaccination and reasons for not wanting to get vaccinated.

Data was analyzed using the software Statistical Package for Social Sciences (SPSS) version 23. Descriptive statistics such frequency and percentage were applied to the variables. Chi-square test was applied to ascertain association with a p-value of <0.05 considered significant.

RESULTS
A total of 108 patients of rheumatoid arthritis were included in the study out of which 80 (74%) were females and 28 (25.9%) were males. The demographic variables of the sample are given in Table-I.

|                | Males | Females | Overall |
|----------------|-------|---------|---------|
| Gender         | 28 (25)| 80 (74) | 108 (100)|
| Mean age (Year)| 43.28 | 42.25   | 42.3    |
| Avg duration of RA (Year) | 3.5    | 4.8     | 4.4     |
| Co-morbidity (%) | 4 (14.2) | 33 (41.2) | 37 (34.2) |
| On DMARDs      | 28 (100)| 80 (100)| 108 (100)|

Table-I. Demographic variables of the study sample.

The influenza vaccination rates reported in the sample were only 3% (n=4). The main reason for not receiving vaccination was lack of awareness as none of the treating doctors had recommended it. 22% patients reported having severe influenza infection during the previous season. Table-II

|                               | Males | Females | Overall |
|-------------------------------|-------|---------|---------|
| Received influenza vaccination n(%) | 4     | 0       | 4 (3)   |
| Ever offered influenza vaccination n(%) | 4     | 0       | 4 (3)   |
| History of influenza infection in previous year n(%) | 12    | 12      | 24 (22) |

Table-II: Vaccination status of the study sample.

All patients were on disease modifying anti-rheumatic drugs (DMARDs). The most common medication was methotrexate 68% (n=73) followed by sulfasalazine 27% (n=30). The distribution of the immunosuppressive drugs being used by the patients in the study is given in the Figure-1.
DISCUSSION
The current study looked at the rates of influenza vaccination in patients of rheumatoid arthritis in Islamabad. To our knowledge, no study has been previously conducted on this topic in Pakistan.

The study shows that influenza vaccination awareness and rates among patients with rheumatoid arthritis is extremely low in our settings. Out of the total 108 patients only 4 patients (3%) had received vaccination. 97% of the patients had no awareness about the need and benefits of vaccination although they had been visiting physicians regularly. Similar work done by Bridges et al in the UK showed significantly higher rates. Out of the total 114 patients included in their study, 73 (57%) had received the influenza vaccine in last twelve months. There were only 5% patients who cited no awareness about the vaccine. A multi-center study conducted by Nguyen et al in Denmark also showed a high number of vaccinations among patients of RA. The study included 192 patients receiving conventional disease-modifying anti-rheumatic drugs (cDMARDs) as well as combination therapy. Their results showed that rate of vaccination against seasonal influenza was 59%.

Studies have proven that influenza vaccination is safe. Rheumatoid arthritis patients, despite being on immunosuppressive medications produce good antibody response. In Pakistan currently there is no influenza vaccination program at national level and majority of people are not aware of the vaccine. We feel that the primary responsibility of educating the patients rests with the medical professionals. Studies have shown that even brief health education sessions can lead to significant improvement in the rates of vaccination. In a study done in Karachi, 87% unvaccinated pregnant women reported willingness to receive vaccination against influenza if recommended by their health care professionals. Study done in Hong Kong by Ka Chun Leung et al demonstrated an increase of 8.6% in uptake of vaccination following a 3 minutes one-on-one verbal health education. One of the limitations of institution-based study such as ours is lack of generalizability to other institutions and areas of the country. The sample size was also small which may yield skewed results. Future studies on the topic should be conducted across multiple centers with a bigger pool of RA patients.

CONCLUSION
The rates of influenza vaccination in patients of rheumatoid arthritis receiving immunosuppressive drugs are extremely low in Islamabad (3% in our study sample). It is high time for the government to adopt a national influenza vaccination program. It is also crucial for healthcare professionals to be aware of the importance of vaccination in RA patients and recommend it during contact with the patients.

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REFERENCES
1. World Health Organization. Influenza (seasonal) factsheet N211 [WHO website]. March, 2014. Available at: http://www.who.int/mediacentre/factsheets/fs211/en/#. Accessed June 6, 2016.
2. Bukhsh A, Rehman H, Mallhi TH, Ata H, Rehman IU, Lee LH, Goh BH, Khan TM. Parents’ attitude, awareness and behaviour towards influenza vaccination in Pakistan. Hum Vaccin Immunother. 2018 Apr 3; 14(4):952-957. doi: 10.1080/21645515.2017.1415686. Epub 2018 Jan 25.
3. Doran MF, Crowson CS, Pond GR, O’Fallon WM, Gabriel SE. Predictors of infection in rheumatoid arthritis. Arthritis and rheumatism. 2002; 46(9):2294–300. Epub 2002/10/02. doi: 10.1002/art.10529 PMID: 12355476.
4. Doran MF, Crowson CS, Pond GR, O’Fallon WM, Gabriel SE. Frequency of infection in patients with rheumatoid arthritis compared with controls: A population-based study. Arthritis and rheumatism. 2002; 46(9):2287–93. Epub 2002/10/02. doi: 10.1002/art.10524 PMID: 12355475.
5. Downey C. Serious infection during etanercept, infliximab and adalimumab therapy for rheumatoid arthritis: A literature review. Int J Rheum Dis. 2016 Jun; 19(6):536-50. doi: 10.1111/1756-185X.12659. Epub 2015 Jul 22.
6. Van Assen S, Agmon-Levin N, Elkayam O, Cervera R, Doran MF, Dougados M, et al. EULAR recommendations for vaccination in adult patients with autoimmune inflammatory rheumatic diseases. Annals of the rheumatic diseases. 2011; 70(3):414–22. Epub 2010/12/07. doi: 10.1136/ard.2010.137216 PMID: 21131643.

7. Holroyd CR, Seth R, Bukhari M, Malaviya A, Holmes C, Curtis E, Chan C. The British Society for Rheumatology biologic DMARD safety guidelines in inflammatory arthritis-Executive summary. Rheumatology (Oxford). 2019 Feb 1; 58(2):220-226. doi: 10.1093/rheumatology/ key207.

8. Influenza and Pneumococcal Vaccination Uptake in Patients with Rheumatoid Arthritis Treated with Immunosuppressive Therapy in the UK: A Retrospective Cohort Study Using Data from the Clinical Practice Research Datalink, https://doi.org/10.1371/journal.pone.0153848.

9. Sowden E, Mitchell WS. An audit of influenza and pneumococcal vaccination in rheumatology outpatients. BMC musculoskeletal disorders. 2007; 8:58. Epub 2007/07/06. doi: 10.1186/1471-2474-8-58PMID: 17610723; PubMed Central PMCID: PMC1949405.

10. Doe S, Pathare S, Kelly CA, Heycock CR, Binding J, Hamilton J. Uptake of influenza vaccination inpatients on immunosuppressant agents for rheumatological diseases: A follow-up audit of the influence of secondary care. Rheumatology. 2007; 46(4):715–6. Epub 2007/01/25. doi: 10.1093/rheumatology/ kel410 PMID: 17244667.

11. Hmamouchi I, Winthrop K, Launay O, Dougados M. Low rate of influenza and pneumococcal vaccine coverage in rheumatoid arthritis: data from the international COMORA cohort. Vaccine. 2015; 33 (12):1446–52.

12. Bridges MJ, Coady D, Kelly CA, Hamilton J, Heycock C. Factors influencing uptake of influenza vaccination in patients with rheumatoid arthritis Ann Rheum Dis. 2003 Jul; 62(7):685.

13. Nguyen M, Lindegaard H, Hendricks O, Friis-Møller N. Factors associated with influenza and pneumococcal vaccine uptake among rheumatoid arthritis patients in Denmark invited to participate in a pneumococcal vaccine trial. Scand J Rheumatol. 2017 Nov; 46(6):446-453. doi: 10.1080/03009742.2016.1242774. Epub 2017 Feb 1.

14. Croce E, Hatz C, Jonker EF, Visser LG, Jaeger VK, Bühler S. Safety of live vaccinations on immunosuppressive therapy in patients with immune-mediated inflammatory diseases, solid organ transplantation or after bone-marrow transplantation - A systematic review of randomized trials, observational studies and case reports. Vaccine. 2017 Mar 1; 35(9):1216-1226. doi: 10.1016/j. vaccine. 2017. 01.048. Epub 2017 Feb 3.

15. Khan AA, Varan AK, Esteves-Jaramillo A, Siddiqui M, Sultana S, Ali AS, Zaidi AK, Omer SB. Influenza vaccine acceptance among pregnant women in urban slum areas, karachi, pakistan. Vaccine. 2015 Sep 22; 33(39):5103-9. doi: 10.1016/j. vaccine. 2015. 08.014. Epub 2015 Aug 18.

16. Leung KC, Mui C, Chiu WY, Ng YY, Chen MHY, Ho PH, Kwok CP, Lam SSM, Wong CY, Wong KY, Pang HH. Impact of patient education on influenza vaccine uptake among community-dwelling elderly: A randomized controlled trial. Health Educ Res. 2017 Oct 1; 32(5):455-464. doi: 10.1093/her/cyx053.

**AUTHORSHIP AND CONTRIBUTION DECLARATION**

| Sr. # | Author(s) Full Name          | Contribution to the paper                                                                 | Author(s) Signature |
|------|------------------------------|------------------------------------------------------------------------------------------|---------------------|
| 1    | Sajid Naseem                 | Conception and design of study. Also designed the data collection from and write up the article.  |
| 2    | Ambreen Zahoor               | Conception and design of study. Also designed the data collection from and write up the article.  |
| 3    | Zaidan Idrees Choudhary      | Interpretation of data and statistical analysis.                                            |
| 4    | Ahmad Bilal Sana             | Interpretation of data and statistical analysis.                                            |