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Knowledge, Degree of Satisfaction, and Practices Regarding Usage of Oseltamivir (Tamiflu) in The Management of Seasonal Influenza Among Health Care Providers in Dubai, UAE



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ABSTRACT

Backgrounds: The influenza virus can cause severe respiratory illness or death in a high-risk population. Oseltamivir (TAMIFLU®) is an influenza neuraminidase inhibitor (NAI) drug that decreases the risk of lower respiratory tract complications, and admittance to the hospital. FDA approved Tamiflu as treatment or as prophylaxis from influenza virus. **Methods:** A cross-section study was conducted to assess the degree of knowledge and Satisfaction regarding the use of the drug among physicians using a validated questionnaire to the physicians. Data was Analysis by using IBM SPSS 27. **Result:** The survey showed that 96% of the healthcare providers had used oseltamivir for their patients. Only 10.4% of the participants were not satisfied and do not recommend oseltamivir for influenza. About 33.86% of them do not recommend oseltamivir as prophylaxis treatment in influenza. The level of the physicians' information about oseltamivir was significantly related to the frequency of the drug usage in influenzas patients (P=0.006) as 94.5%, 77.3%, and 84.7% had moderate to good knowledge about oseltamivir treatment, prophylaxis, and general respectively. The physicians with higher designations have more knowledge and were more satisfied and recommend oseltamivir. **Conclusion:** This research reveals that the knowledge is directly proportional to the usage of the drug in their practice. It is recommended that all physicians should be updated with the recent guidelines regarding the management of the influenza virus. Clinical Pharmacists should conduct medication updates to all healthcare providers with evidence-based literature to rationalize medication use.



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INTRODUCTION

Globally millions are infected with the influenza virus, and about half a million people die each year because of its' complications. Influenza virus can be treated by using antivirals or prevented by using Antivirals, and influenza vaccines. (1-3)Influenza virus has a high mutation rate, that's why using the influenza vaccine that has been invented since the 1940s as prevention is not very efficient. (4)Oseltamivir (TAMIFLU®) is an influenza neuraminidase inhibitor (NAI)that inhibits influenza virus neuraminidase and shows its beneficial effect against the influenza virus. FDA approved Tamiflu to treat influenza virus in adults and children ages2 weeks old and older who have had symptoms for less than two days..(5-8). Oseltamivir is a lifesaving drug from influenza virus in special populations and decreases the duration of the disease. (9)(10). So, it is important to assess the knowledge and degree of satisfaction among healthcare providers for using this drug in influenza patients, to emphasize the significant benefits of Tamiflu, and to encourage rational use of oseltamivir.

Methodology

Ethical considerations:

This study was approved by Dubai pharmacy college research ethical committee (DPC-REC), Aster Hospital, and by Dubai health authority (DHA) ethical committee; University Student and Resident Research Committee (USRRC), and Medical Education and Research Department (MERD), UAE.

Data validation and reliability:

A standard questionnaire was developed using authenticated and updated information about oseltamivir. The questionnaire was validated with a group of experts and collected their feedback and suggestion to improve the questionnaire. A pilot study was conducted to check the reliability of the response using the Cronbach alpha test.

Survey questionnaires contents:

Section 1 (demographic information), Section 2 (recommendation and satisfaction) consists of two parts: Part A: Oseltamivir Treatment, and Part B: Oseltamivir as prophylaxis. And Section 3 (knowledge of physicians) consists of three parts: Part A "If Tamiflu is used in the treatment of influenza virus", Part B "If Tamiflu is used as prophylaxis in influenza virus", Part C "general information's of oseltamivir".

Study design & Sample size:

A cross-sectional descriptive study was conducted among physicians by distributing the survey through email. A follow-up was done to collect the response with the desired number needed based on the sample size calculator(11)and about 75 had complete retort while achieving a 93.75% response rate.

Data Analysis:

The data were analyzed by using IBM SPSS software, version 27. Descriptive statistics were obtained with the frequency and percentage of each response. A Chi-square test was performed to compare the level of satisfaction, recommendation, and knowledge with their demographic data and the of the drug. Stem and leaf plots were obtained to compare their knowledge and practice with their satisfaction with treatment.

RESULTS

From 80 participants, a total of 75 healthcare providers completed the questionnaire and were enrolled in this study. The demographic data of the participants are presented in Table-1. A majority of the healthcare providers were Indians 65 (86.7%), then Pakistanis 8 (10.7%), and Egyptians 2 (2.7%). Medical certificate origin countries were from India 65 (86.7%), Pakistan 7 (9.3%), Egypt 2 (2.7%), and UAE 1 (1.3%). Regarding the age group, 33 (44%) were less than 40 years old, 32 (42.7%) were between 41-51 years old, and 10 (13.3%) were more than 50 years old. There were about 22 (29.3%) General practitioner or family medicine physicians, 22 (29.3%) Internal medicine physicians, 16 (21.3%) pediatricians, and 15 (20%) Gynecologist in this study. The last degree of qualifications for participants were MBBS-17 (22.7%), M.D.-48 (64%), and Fellowship-10 (13.3%). The majority 72 (96%) of participants were prescribing Oseltamivir (Tamiflu) in their practice. Regarding the frequent use of Oseltamivir (Tamiflu) among physicians, 3 (4%) stated that they Always use Oseltamivir (Tamiflu) in their practice, and 6 (8%) of them are rarely using Oseltamivir (Tamiflu) in their practice. Most of them answered often 38 (50.7%) and sometimes 28 (37.3%) regarding using Oseltamivir (Tamiflu) in their practice.

Table no 1: Demographic information

Variables	N (%)
Age group	
< 40	33 (44%)
41-50	32 (42.7%)
> 50	10 (13.3%)
Nationality	
India	65 (86.7%)
Pakistan	8 (10.7%)
Egypt	2 (2.7%)
Last degree of qualifications	
MBBS	17 (22.7%)
M.D.	48 (64%)
Fellowship	10 (13.3%)
Medical certificate origin country	
India	65 (86.7%)
Pakistan	7 (9.3%)
Egypt	2 (2.7%)
UAE	1 (1.3%)
Profession	
General practitioner/family medicine physician	22 (29.3%)
Internal medicine physician	22 (29.3%)
Pediatrician	16 (21.3%)
Gynecologist	15 (20%)
Have you ever prescribed Oseltamivir (Tamiflu) in your practice?	
Yes	72 (96%)
No	3 (4%)
How frequently do you use Oseltamivir (Tamiflu) in your practice?	
Often	41 (54.7%)
Sometimes	28 (37.3%)
Rarely	6 (8%)

Most of the participants have been agreed to various statements regarding satisfaction and recommendation of Tamiflu as treatment or prophylaxis. Satisfaction and recommendation of Tamiflu as treatment/prophylaxis statements are found in Table-2. About 89.6% of the healthcare providers are satisfied and recommend oseltamivir as a treatment for the influenza

virus and 10.4 % of them are not satisfied and do not recommend oseltamivir for the treatment of influenza. For prophylaxis treatment, 33.86% of them do not recommend oseltamivir as a precaution for the influenza virus.

Table no 2: Satisfaction and Recommendation of Tamiflu as treatment

Part A: Oseltamivir (TAMIFLU) as Treatment	Satisfied and recommend	Not satisfied and Do not recommend
Questions	Agree	Disagree
Q1. I generally recommend using Tamiflu, as a treatment for influenza.	69 (92%)	6 (8%)
Q2. I believe that Tamiflu should be prescribed for all patients having influenza.	61 (81.3%)	14 (18.7%)
Q3. I believe that Tamiflu should be prescribed against influenza for children less than five years old, elderly, and pregnant women.	71 (94.7%)	4 (5.3%)
Q4. I believe that Tamiflu should be prescribed against influenza for asthmatic and immunocompromised patients.	74(98.7%)	1 (1.3%)
Q5. I am satisfied regarding the effectiveness of Tamiflu as treatment from influenza virus.	61 (81.3%)	14 (18.7%)
Overall Satisfaction	67.2 (89.6%)	7.8 (10.4%)
Part B : Oseltamivir (TAMIFLU) as Prophylaxis	Satisfied and recommend	Not satisfied and Do not recommend
Q6. I generally recommend using Tamiflu, as prophylaxis from influenza virus.	44 (58.7%)	31 (41.3%)
Q7. I believe that Tamiflu should be prescribed as prophylaxis for all people who are in close contact with infected influenza virus patients.	38 (50.7%)	37 (49.3%)
Q8. I believe that Tamiflu should be prescribed as prophylaxis for children less than five years old, elderly, and pregnant women who are in close contact with infected influenza virus patients.	49 (65.3%)	26 (34.7%)
Q9. I believe that Tamiflu should be prescribed as prophylaxis for asthmatic and immunocompromised patients who are in close contact with infected influenza virus patients	64 (85.3%)	11 (14.7%)
Q10. I am satisfied regarding the effectiveness of Tamiflu as prophylaxis from influenza virus.	53 (70.7%)	22 (29.3%)
Overall Satisfaction	49.6 (66.14%)	25.4 (33.86%)

Section C consists of three parts, Part A: If Tamiflu is used in the treatment of influenza virus, Part B: If Tamiflu is used in prophylaxis of influenza virus, and Part C: knowledge of physicians regarding general information of Oseltamivir (Tamiflu). Each of the first two parts has 4 questions. If the answer of the physician is right, he or she will take one point, and will take zero points if the answer is wrong. If the physician's total knowledge score is 3 or more out of four that means the physician has good knowledge. If the physician's total score is 2, that means the physician has moderate knowledge. And if the total knowledge score is less than 2 out of four, that means the physician has poor knowledge. Part C has six questions. If the answer of the physician is right, he or she will take one point, and will take zero points if the answer is wrong. If the total physician knowledge score is 5 and more out of six, that means the physician has good knowledge. If the physician's total score is 3 or 4 out of six that means the physician has moderate knowledge. And if the total knowledge score is 2 or less out of six, that means the physician has poor knowledge.

Regarding the first two parts, most of the participants have chosen the right answers to Tamiflu's questions if it is used as treatment or prophylaxis. Knowledge questions for physicians regarding Tamiflu, if it is used as Treatment or as prophylaxis are found in Table - 3. Part A (If Tamiflu is used in the treatment of influenza virus) consists of four questions. The first question is regarding the best timing to give Tamiflu, and 62 (82.7%) choose the right answer which is within the first 48 hours from influenza symptoms appearance. The second question is regarding the dose of Tamiflu, and 65 (86.7%) chooses the right answer which is 75mg twice daily. The third question is regarding the duration of using Tamiflu, and 71 (94.7%) choose the right answer which is Five days. The fourth question is regarding the age where Tamiflu can be given, and 34 (45.3%) choose the right answer which is > two weeks. Part B (If Tamiflu is used as prophylaxis from influenza virus) consists of four questions. The first question is regarding the best timing to give Tamiflu, and 53 (70.7%) choose the right answer which is Within 48 hours following close contact with an infected individual. The second question is regarding the dose of Tamiflu, and 40 (53.3%) choose the right answer which is 75mg once daily. The third question is regarding the duration of using Tamiflu, and 37 (49.3%) choose the right answer which is ten days. The fourth question is regarding the age where Tamiflu can be given, and 38 (50.7%) choose the right answer which is > one year.

Table no 3: Knowledge of physicians regarding Tamiflu, if it used as Treatment or as prophylaxis

Variables	N (percentage %)		
Questions	Response		
Q1. Which time is the best to give Tamiflu?	within the first 12 hours from influenza symptoms appearance	within first 48 hours from influenza symptoms appearance*	after 48 hours from influenza symptoms appearance
	13 (17.3%)	62 (82.7%)	0 (0.0%)
Q2. What is the dose of Tamiflu?	75mg once daily	75mg twice daily*	75mg three times daily
	10 (13.3%)	65 (86.7%)	0 (0.0%)
Q3. What is the duration of using Tamiflu?	Two days	Five days *	Ten days
	0 (0.0%)	71 (94.7%)	4 (5.3%)
Q4. At which age Tamiflu can be given?	> two weeks*	> six months	> one year
	34 (45.3%)	11 (14.7%)	30 (40%)
Questions	Response		
Q1. Which time is the best to give Tamiflu?	Within 12 hours following close contact with an infected individual.	Within 48 hours following close contact with an infected individual.*	Within 72 hours following close contact with an infected individual.
	18 (24%)	53 (70.7%)	4 (5.3%)
Q2. What is the dose of Tamiflu?	75mg once daily*	75mg twice daily	75mg three times daily
	40 (53.3%)	35 (46.7%)	0 (0.0%)
Q3. What is the duration of using Tamiflu?	Two days	Five days	Ten days*
	0 (0.0%)	38 (50.7%)	37 (49.3%)
Q4. At which age Tamiflu can be given?	> two weeks	> six months	> one year*
	8 (10.7%)	29 (38.7%)	38 (50.7%)

(*): Right answer

Part C (knowledge of physicians regarding general information of Oseltamivir (Tamiflu)) consists of six questions. The Knowledge questions for physicians regarding general information of Oseltamivir (Tamiflu) are found in Table-4. The first question is regarding the mechanism of action, and 57 (76%) choose the right answer which is Neuraminidase inhibitors. The second question is regarding the most common side effect of

Tamiflu, and 75 (100%) choose the right answer which is GI side effects (Nausea and Vomiting). The third question is regarding the doses in special populations, and it consists of four parts labeled as A, B, C, and D. question A is regarding dose modification for pregnant women if it is required, 43 (57.3%) choose the right answer which is “yes, it is required”. Question B is regarding dose modification based on BMI if it is required, and 40 (53.3%) choose the right answer which is “No it is not required”. Question C is regarding dose modification for patients with renal impairment if it is required, and 59 (78.7%) choose the right answer which is “yes, it is required”. Question D is regarding dose modification for patients with hepatic impairment if it is required, and 18 (24%) choose the right answer which is “No it is not required”.

Table no 4: Knowledge of physicians regarding general information’s of Oseltamivir (Tamiflu)

Variables	N (%)		
Questions	Response		
Q1. What is the mechanism of action of Tamiflu?	Nucleoside Reverse Transcriptase inhibitors	Neuraminidase inhibitors*	Protease inhibitors
	11 (14.7%)	57 (76%)	7 (9.3%)
Q2. What is the most common side effect of Tamiflu?	GI side effects (Nausea & Vomiting)*	Neuropsychiatric events (confusion &hallucination)	Hypersensitivity (anaphylaxis& swollen tongue)
	75 (100%)	0 (0.0%)	0 (0.0%)
Q3. Doses for special populations	Yes	Not sure	No
A. Do you recommend the dose modification of Tamiflu for pregnant women?	43 (57.3%)*	25 (33.3%)	7 (9.3%)
B. Do you recommend the dose modification of Tamiflu based on BMI?	11 (14.7%)	24 (32%)	40 (53.3%)*
C. Do you recommend the dose modification of Tamiflu for patients with renal impairment?	59 (78.7%)*	12 (16%)	4 (5.3%)
D. Do you recommend the dose modification of Tamiflu for patients with hepatic impairment?	32 (42.7%)	25 (33.3%)	18 (24%)*

(*): Right answer

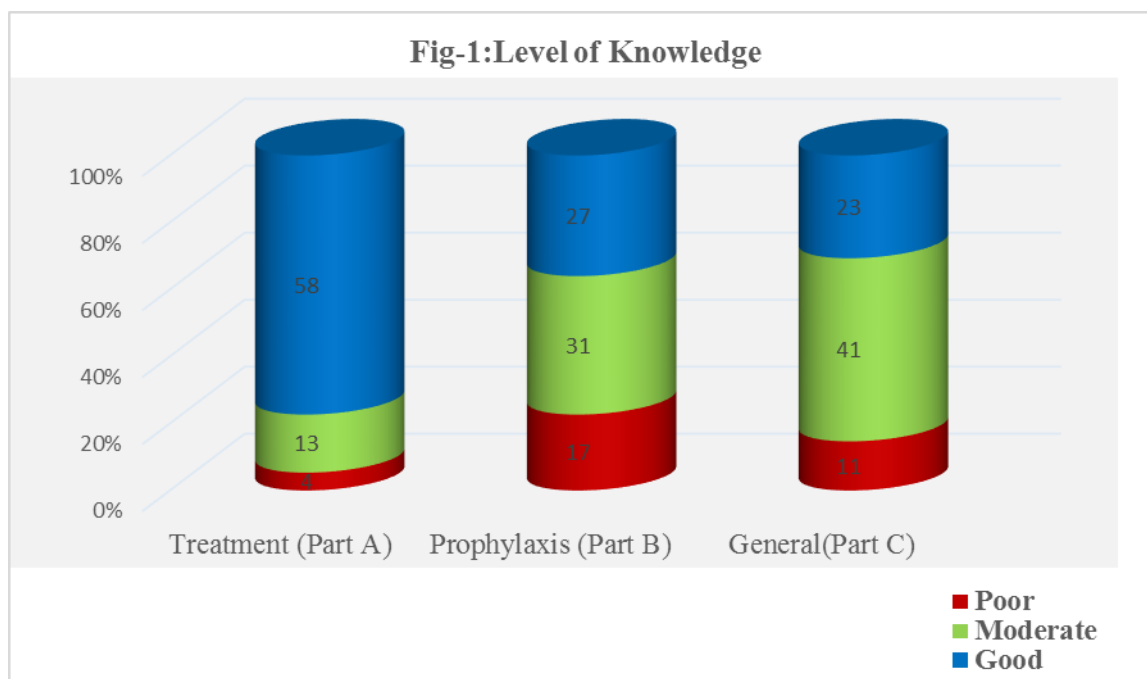


Figure no-1 shows the physicians' level of knowledge regarding using Tamiflu as treatment, using Tamiflu as prophylaxis, and Tamiflu general information level. For part A (Tamiflu treatment questions), the majority of the participants 58 (77.3%) have overall good knowledge. And for part B (Tamiflu prophylaxis questions), the majority of the Participants are having overall moderate knowledge 31 (41.3%), and overall good knowledge 27 (36%), respectively. For part C (Tamiflu general information questions), the majority of participants are having overall moderate general knowledge 41 (54.7%). and overall good general knowledge 23 (30.7%), respectively.

The data in figure 2 represent the total knowledge of physicians with the frequency of using Tamiflu. 41 (54.7%) of the participants were having moderate knowledge. 19 (25.3%) of the participants were having poor knowledge. And 15 (20%) of the participants were having good knowledge.

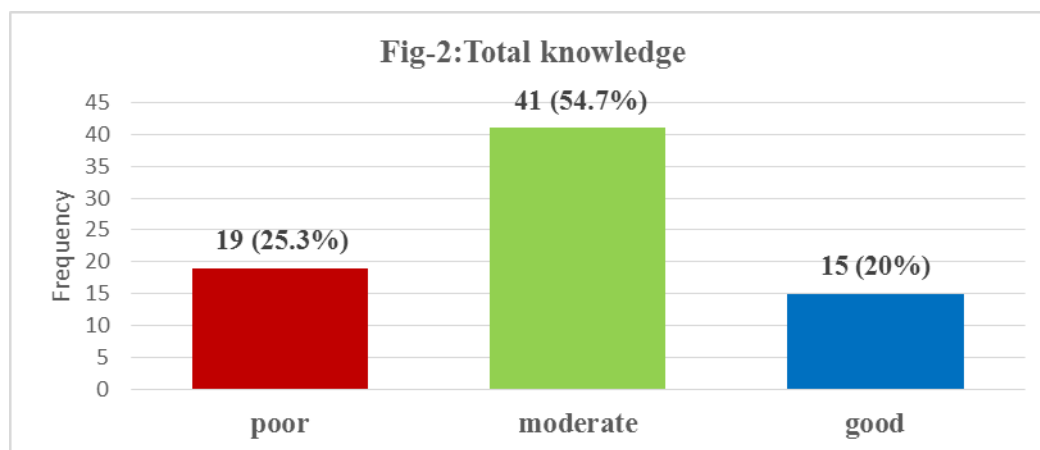


Table no 5: Comparison of Total Knowledge with the frequency of use

Level of Knowledge	Frequently	Sometimes	Rarely	Total
Poor knowledge	5	9	5	19
Moderate knowledge	25*	15	1	41
Good knowledge	11	4	0	15
Total	41	28	6	75

Chi square test, P-Value-0.006*

The results mention in table 5 shows the comparison of total knowledge of oseltamivir and the frequency of usage of the drug. The data reveals that the knowledge of the drug is directly proportional to the usage of the drug. The more they use the drug, the more is the increase in their knowledge of the drug. Out of 41 participants who use the drug more frequently, 36 (86.9%) of them had moderate to good knowledge and only 5(13.1%) have poor knowledge. when chi-square was applied to the comparison of frequencies, the group with frequency use had a significant difference P-value-0.006) when compared to other groups.

When the total knowledge was compared to the qualification/ designation of the participants, it was found that the healthcare provider has the highest qualification or designation had more knowledge when compared to other counterparts. The data in fig-3 represent the stem and leaf distribution of knowledge and qualification among different groups. The average knowledge of physicians with fellowship was about (10.8/14)77.14% followed by physicians with MD degrees (9.2/14)65.7% and least was with basic degree MBBS (8.3/14)59.2%.

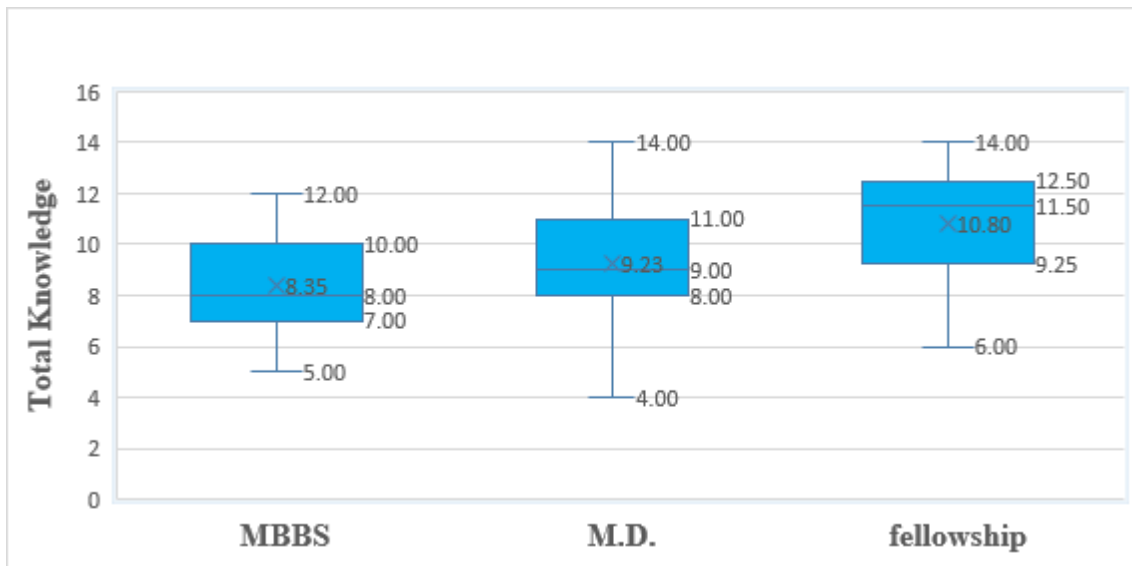


Figure no 3: Comparison of Total Knowledge and Qualification/Designation

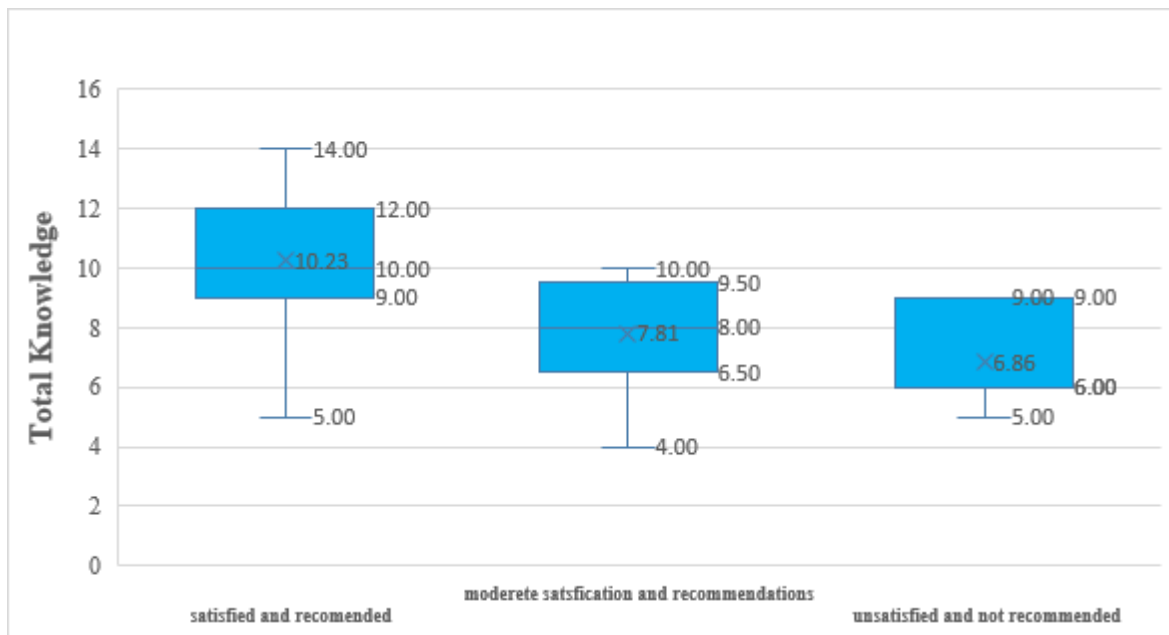


Figure no 4: Comparison of Total Knowledge and Satisfaction

The data in fig-4 represents the stem and leaf distribution of knowledge and satisfaction level of participants regarding Tamiflu. The participants who are more satisfied and recommend Tamiflu in the treatment of influenza had more knowledge. The participants who are more satisfied, moderately satisfied, and not satisfied had 72.85%, 55.71%, and 48.57% of knowledge respectively.

DISCUSSION

Regarding the frequent use of Oseltamivir, most of the physicians were often prescribed Oseltamivir (Tamiflu) in their practice (38/75; 50.7%). This percentage was comparable and similar to a prospective study, that was conducted by Vardakas et al. 2016 (12), which showed that 46% of patients infected with the influenza virus, have received Oseltamivir, according to physicians' prescription. Regarding the last degree of qualifications, M.D. qualified physicians have the highest response (64%), then MBBS physicians (22.7%), and the lowest response was for fellowship physicians (13.3%). These findings were comparable and similar to a study that was conducted by Justin R. Ortiz et al. 2008. (13) Which showed that the most respondents and the most physicians that prescribed Tamiflu during 2005 were M.D. qualified physicians (44%), then MBBS physicians (30.5%), and the lowest responses were for fellowship physicians (25.6%).

In 2005, media reports about the influenza pandemic have been increased, and due to this, prescribing Oseltamivir as treatment has been increased among physicians with different specialties (General medicine, infectious disease, family medicine, pediatrician, adult specialty, and pediatric specialty, respectively) through 2004- 2005, especially for patients with high age (> 50), chronic diseases and pulmonary diseases. Because of this, knowledge of physicians and practices regarding Oseltamivir has been increased. (13). So, inconsistent with the previous research mentioned, the result of the current research shows that physicians who are often and sometimes using Tamiflu as treatment is having good knowledge, while physicians who are rarely using Tamiflu as treatment are having moderate knowledge and poor knowledge. These results justified that the physicians who prescribe Tamiflu more frequently as treatment, are having updated information on Tamiflu. These results justified that the physicians who prescribe Tamiflu more frequently, need to stay updated with recent information regarding this medication for the patients' safety, and as a result, they will have adequate knowledge of Tamiflu.

Recent studies showed that influenza vaccines will reduce illness between 40%-60% among all populations during influenza seasons, while antiviral drugs including Oseltamivir will prevent influenza from 60%-90% (14)(15) But, H1N1 influenza A viruses has shown resistance to Oseltamivir (Tamiflu) in 2007, due to H275Y mutation, and were present at high rates during 2008-2009 influenza season. (16) Another study was conducted among UK physicians regarding the use of NAIs for patients with suspected influenza virus. And it

shows that lack of confidence regarding the effectiveness of NAIs, lack of knowledge, and adherence to current management guidelines, will limit the use of those medications as prophylaxis. (17) So inconsistent with the previous research mentioned, the results of this research showed that most physicians have overall moderate knowledge of Tamiflu as prophylaxis, are moderately satisfied, and recommend Tamiflu as prophylaxis 19/31 (61.3%). while most physicians who have good knowledge are also moderately satisfied and recommend Tamiflu as prophylaxis 14/27 (51.8%). The physicians who have poor knowledge, are unsatisfied and do not recommend Tamiflu 11/17 (64.7%). So, this can be justified by lack of confidence, lack of knowledge and information regarding the of NAIs effectiveness against influenza virus as prophylaxis, or regarding being afraid of Oseltamivir (Tamiflu) resistance, will lead to decrease satisfaction and recommending Tamiflu as prophylaxis.

A retrospective multicenter study included 1828 adult hospitalized influenza patients from two major teaching hospitals in Australia and was taken between January 2016-March 2020. Patients who received Oseltamivir < 48 hours of admission were compared with those who either did not receive treatment or if treatment was delayed by >48 h. the results showed that Early administration of Oseltamivir was associated with a reduction in 30- days readmissions and mortality than those who did not take oseltamivir or delay in treatment. (18) Also a cross-sectional, multiple-choice, open responded survey was conducted among 70 adult patients and adult caregivers of pediatric patients who have flu-like symptoms and took and prescribed for them oseltamivir (Tamiflu) as treatment at rural emergency, during the 2014-2015 flu season department. Most of them reported positive expectations regarding the efficacy of oseltamivir (Tamiflu) and overstated that oseltamivir (Tamiflu) is an effective treatment. And this is because of the physicians' adequate knowledge and satisfaction regarding the effectiveness of this medication, which led to giving positive expectations to their patients. (19) On the other hand, A cross-sectional study was conducted among physicians in Seth GSMC and KEM hospital, Mumbai, in July 2017. It stated in the infection control H1N1 portion, that 52.9% of physicians would start oseltamivir therapy as a treatment after 2 days of onset of symptoms, 25% preferred not to take any medicine, and only 21% of physicians would start oseltamivir (Tamiflu) with 48 hours from onset of the symptoms. As a result, a lack of knowledge of physicians' information regarding oseltamivir will lead to developing resistance to the drug, thus less efficacy for treating the disease, and the satisfaction and recommendation of oseltamivir will be decreased. (20) Inconsistent with the

previous research mentioned the results of this research show that the majority of physicians who have overall good knowledge of Tamiflu as treatment are satisfied and recommend Tamiflu.

A study was made to test the information of health care providers before giving information regarding oseltamivir and after giving information regarding oseltamivir. The questions were about Oseltamivir's medication classification, mechanism of action, the timeframe in which to prescribe this medication, medication resistance, and considerations of oseltamivir in special populations including patient's age, patient's weight, patient's renal function, and other health conditions to be considered, the results showed that the health care providers have a clear understanding after giving the information to them, and made their post-test. (21) So inconsistent with the previous research mentioned, the results of this research showed that the majority of physicians who have overall moderate knowledge regarding general information's of oseltamivir, are satisfied and recommend Tamiflu as treatment, while most of the physicians who have good knowledge regarding general information's of oseltamivir are also satisfied and recommend Tamiflu as a treatment for influenza.

CONCLUSION

This study reveals that there is a significant difference in the drug information of Tamiflu which has an influence on the use of the drug in the treatment or uses it as prophylaxis in influenzas. Physicians who use the drug frequently have a good satisfaction level and who use rarely are not satisfied with the use of the drug in influenza. There is a need for a clinical pharmacist to conduct awareness programs of evidence-based medicines to the physicians regarding using Tamiflu as prophylaxis and to stay updated with the recent guidelines regarding the management of the influenza virus.

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