Original Reserach Article

Assessment of prevalence of SARS-CoV-2 Infection in patients on anti-HBV (lamivudine) treatment: A questionnaire based survey

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ABSTRACT

Introduction: COVID 19 Pandemic has compelled researchers to revisit available resources for treating these patients. Coronavirus disease (COVID-19) is an infectious disease caused by the Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2). Lamivudine is the antiviral drug used for treatment of Hepatitis-B, HIV-1 and HIV-2 infection.

Aims and objectives: We hypothesise that Lamivudine, may play a role as an effective agent in SARS-CoV-2 infection. This is just a pilot study to explore if there is any relation between the two.

Materials and Methods: A retrospective study was undertaken through questionnaire-based survey. 100 patients with HBV infection taking Lamivudine treatment were selected. All patients were consecutively enrolled in this study and informed consent was obtained.

Results: About 70% of the participants in the Lamivudine group had no fever. Around 59.4% were having fever in the Non-Lamivudine group. The association between presence or absence of fever among family/friends and type of group was assessed. It was found that all the participants in the Non-Lamivudine group (411) and Lamivudine group (100) had fever. Though the percentage of fever was less in the Lamivudine group. The association between home/office in containment zone and type of group was assessed. It was observed that all the participants in both the groups had their home/offices in the containment zone. 43% of the participants in the Lamivudine group had history of domestic travel after 1st march 2020 while 74% had history of domestic travel after 1st march 2020 in the Non-Lamivudine group. 56% of the participants in the Lamivudine group had come in contact with COVID-19 suspected/infected individual as compared to 65.7% in Non-Lamivudine group who had come in contact with COVID-19 suspected/infected individual. 66% of the participants in the Lamivudine group were undergoing preventive medicine for COVID-19 infection & 54.3% of the participants were undergoing preventive medicine for COVID-19 infection in the Non-Lamivudine group. 49% of the participants in the Lamivudine group did not have any other co-morbidities as compared to 63.3% in the Non-Lamivudine group. About 2% of the participants in the Lamivudine group were COVID positive as compared to 48.4% of the participants were COVID positive in the Non-Lamivudine group. There are lower chance of .0217 times of having COVID positive in individuals with Lamivudine medication in comparison of individuals without Lamivudine medication and this association is statistically significant (p< 0.0001).

1. Introduction

Coronavirus disease (COVID-19) is an infectious disease caused by the Severe Acute Respiratory Syndrome

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Coronavirus-2 (SARS-CoV-2) formerly known as the 2019 novel Coronavirus (2019 nCoV).[1,2] The virus originated in bats and was transmitted to humans through pangolin or other wild animals in Wuhan, Hubei province, China in December 2019.[1,3] The main pathogenesis of COVID-19 infection as a respiratory system targeting virus was severe pneumonia, viremia, combined with the incidence of ground-glass opacities, and acute cardiac injury. Significantly high blood levels of cytokines and chemokines were noted in patients with COVID-19 infection that included IL1-β, IL1RA, IL7, IL8, IL9, IL10, basic FGF2, GCSF, GMCSF, IFNγ, IP10, MCP1, MIP1α, MIP1β, PDGFB, TNFα, and VEGFA.[4,5]

Corona virus contains four main structural proteins; spike (S), membrane (M), envelope (E), and nucleocapsid (N) proteins are encoded by ORFs 10, 11 on the one-third of the genome near the 3′-terminus.[6] Structural similarity between HIV-1 gp41 and SARS-CoV-2 spike protein S2 is documented.[7] These two proteins share the same two α helices, suggesting that the two viruses could follow an analogous membrane fusion mechanism.[7]

As corona virus shows structural similarities with HIV, this may have a potential to be employed as a Preventive/Therapeutic agent against SARS-CoV-2. Studies have shown structural similarities between HIV and SARS-CoV-2 as they share the same two α helices in gp41 & SARS-CoV-2 S2 share the, suggesting that the two viruses could follow an analogous membrane fusion mechanism. Ligand-binding analysis has also shown that two inhibitors GGL and D-peptide from HIV-1 gp41 may serve as inhibitors for SARS-CoV-2 entry.[8] We hypothesise that Lamivudine, may be an effective agent against both HBV and HIV, hence it may be taken into consideration with SARS CoV-2. whether individuals already on Lamivudine therapy for HBV are having any role in the infection with SARS CoV-2?. This is just a pilot study to explore if there is any relation between the two.

2. Materials and Methods

A retrospective study was undertaken through-2 questionnaire-based survey. The power of the study was at 80% and sample size was calculated with OpenEpi software for case control study. The study was ethically approved by the institutional ethics committee.

100 patients with HBV infection on Lamivudine treatment were selected. All patients were consecutively enrolled in this study and informed consent was obtained.

2.1. Inclusion criteria

All Hepatitis B positive cases on Lamivudine therapy.

2.2. Enrolment

Individuals in the study groups comprise of HBV infected ones on Lamivudine treatment. They have been on this treatment for more than 5 years and will be under the supervision of their respective physicians. Further study population comprise of individuals with or without vitamin supplements and with and without flu vaccination. For the comparison of the response to Lamivudine therapy cases, selective controls were matched according to gender and age for this case-control study.

2.3. Allocation

The study population was divided into two groups as follows:

Group 1-Cases: Adult individuals with HBV infection and on Lamivudine therapy will form a subgroup Cases-1, Individuals on multivitamin supplements as subgroup Cases -2.100 cases were selected and informed consent was obtained from them.

Group 2- Controls: The family members of the patients that are not infected with HBV and are not on Lamivudine therapy, not on multivitamin supplements and had not taken flu vaccine will be used as respective controls. With a ratio of 4:1, 400 controls were selected for the study.

2.4. Matching

Individual matching was done for the cases and controls to avoid confounding bias.

2.5. Test

A feedback form (questionnaire) from each participant was taken for both HBV and SARS-CoV-2 infection, status of multivitamin consumption. The questionnaire was pre-designed, and pre-validated by the subject experts. The questionnaire was drafted, validated and checked for feasibility and reproducibility by a pilot run. The questionnaire was taken via mobile phones on a no physical contact basis.

2.6. Questionnaire

It consisted of two sub-sections, initial demographic details and medical history, which included the drug history and SARS-CoV-2 infection. The second part had 4 questions which were probing type having dichotomous response.

2.7. Evaluation

The results obtained from the qualitative tests (feedback/ questionnaire) were recorded and analysed for the evaluation of the study.

2.8. Analysis

The obtained data was subjected to statistical analysis using SPSS software. Descriptive statistics was performed for both the sections of the questionnaire with chi square test mentioned in Table 1. Inferential statistics were drawn for measuring the association between the case and controls with 95% confidence interval. A p-value less than 0.05 was regarded as statistically significant. (Table 1)

3. Results

About 70% of the participants in the Lamivudine group had no fever. Around 59.4% were having fever in the non-Lamivudine group. The association between presence or absence of fever among family/friends and type of group was assessed. It was found that all the participants in the Non-Lamivudine group (411) and Lamivudine group (100) had fever. Though the percentage of fever was less in Lamivudine group, association between home/office in containment zone and type of group was assessed. It was observed that all the participants in both the groups had their home/offices in the containment zone. 43% of the participants in the Lamivudine group had history of domestic travel after 1st march 2020 while 74% had history of domestic travel after 1st march 2020 in the non-Lamivudine group. About 74% of the participants in the Lamivudine group had gone out of house during lockdown; compared to 63.5% of the participants from non-Lamivudine group who had gone out of house. 56% of the participants in the Lamivudine group had come in contact with COVID-19 suspected/infected individual as compared to 65.7% in Non-Lamivudine group who had come in contact with COVID-19 suspected/infected individual. 66% of the participants in the Lamivudine group were undergoing preventive medicine for COVID-19 infection & 54.3% of the participants were undergoing preventive medicine for COVID-19 infection in the Non-Lamivudine group. 49% of the participants in the Lamivudine group did not have any other co-morbidities as compared to 63.3% in the Non-Lamivudine group. All the participants in the Lamivudine group had undergone test for hepatitis, whereas no participant from Non-Lamivudine group was tested for hepatitis. All the participants in the Lamivudine group were taking Lamivudine, whereas participants in the Non-Lamivudine group were not taking Lamivudine. About 2% of the participants in the Lamivudine group were COVID positive as compared to 48.4% of the participants were COVID positive in the Non-Lamivudine group.

4. Odd's Ratio

Cases with positive (bad) outcome
Number in exposed group: 2 (a)
Number in control group: 199 (c)
Cases with negative (good) outcome

Number in exposed group: 98 (b)
Number in control group: 212 (d)

Odds of an event happening is defined as the likelihood that an event will occur, expressed as a proportion of the likelihood that the event will not occur. OR <1 indicates decreased occurrence of an event (protective exposure). An odds ratio is less than 1 is associated with lower odds. There are lower chance of .0217 times of having COVID positive in individuals with Lamivudine medication in comparison of individuals without Lamivudine medication and this association is statistically significant (p< 0.0001)

5. Discussion

The entire world is going through a very tough time indeed due to COVID-19 pandemic. COVID-19 is an infectious disease that has asserted its presence globally and has led to a newer and faster research activity in the field of its treatment, development of effective therapeutic agents as well as vaccines. Non availability of specific treatment and vaccines has led medical researchers to revisit the antiviral repositories, including the ones that have been used for some other viral infections like HIV, HBV etc. (re-purposive drugs). The present study is focused on the role of Lamivudine with relation to SARS-CoV-2.

The results of the present study demonstrate that there are lower chances of (OD ratio 0.0217) of having COVID positivity (only 2% in L group than 48% in NL group) in Lamivudine medication and this association is statistically significant P < 0.001 [Table 3].

The majority of the participants in the study group 2 were exposed in their respective environments without any isolation or quarantine & therefore had high chances of contacting the virus. [Table 2]

The individuals in Lamivudine group had hepatitis and were tested positive for HBV surface antigen, and HBV-DNA. The average duration of Lamivudine consumption was about 3-5 years and the average dose as prescribed by their physician was about 100mg/day. As mentioned earlier the antiviral medicine Lamivudine has been used effectively for treating HBV and may have some role in preventing the spread of COVID infection that is what is probed qualitatively in this study.

At present, there are no specific antiviral drugs or vaccine against COVID-19 infection for potential therapy for humans. The only option available is using broad-spectrum antiviral drugs like nucleoside analogues and also HIV-protease inhibitors that could attenuate virus infection until the specific antiviral becomes available.[4] L-Nucleoside analogue like Lamivudine has been commonly used as a cost-effective therapy for hepatitis especially HBV infection. Long term (5-10yrs) use of Lamivudine has shown HBV suppression and HBsAg seroclearance.[6] These antiviral compounds have been used in human patients with a safe track record. Thus, these therapeutic agents

Table 1: Association between individual question-responses and type of Group involved

| | | | Group | | Total | p value |
			Non-Lamivudine	Lamivudine		
Fever	Absent	n%	167(40.6%)	70(70.0%)	237(46.4%)	.000*
	Present	n%	244(59.4%)	30(30.0%)	274(53.6%)	
Total		n%	411(100.0%)	100(100.0%)	511(100.0%)	
Fever among Family/Friends	Present	n%	411(100.0%)	100(100.0%)	511(100.0%)	.000*
Total		n%	411(100.0%)	100(100.0%)	511(100.0%)	
Home/Office in Containment Zone	Yes	n%	411(100.0%)	100(100.0%)	511(100.0%)	.000*
Total		n%	411(100.0%)	100(100.0%)	511(100.0%)	
Domestic Travel after 1st March 2020	No	n%	103(25.1%)	57(57.0%)	160(31.3%)	.000*
	Yes	n%	308(74.9%)	43(43.0%)	351(68.7%)	
Total		n%	411(100.0%)	100(100.0%)	511(100.0%)	
Gone out of house during Lockdown	No	n%	150(36.5%)	26(26.0%)	176(34.4%)	.060
	Yes	n%	261(63.5%)	74(74.0%)	335(65.6%)	
Total		n%	411(100.0%)	100(100.0%)	511(100.0%)	
Incurred Contact with COVID -19 suspected /infected individual	No	n%	141(34.3%)	44(44.0%)	185(36.2%)	.082
	Yes	n%	270(65.7%)	56(56.0%)	326(63.8%)	
Total		n%	411(100.0%)	100(100.0%)	511(100.0%)	
Undergoing Preventive Medicine for COVID - 19 Infection	No	n%	188(45.7%)	34(34.0%)	222(43.4%)	.043*
	Yes	n%	223(54.3%)	66(66.0%)	289(56.6%)	
Total		n%	411(100.0%)	100(100.0%)	511(100.0%)	
Any other medical conditions	Absent	n%	151(36.7%)	49(49.0%)	200(39.1%)	.030*
	Present	n%	260(63.3%)	51(51.0%)	311(60.9%)	
Total		n%	411(100.0%)	100(100.0%)	511(100.0%)	
Test for hepatitis	No	n%	411(100.0%)	0(0.0%)	411(80.4%)	.000*
	Yes	n%	0(0.0%)	100(100.0%)	100(19.6%)	
Total		n%	411(100.0%)	100(100.0%)	511(100.0%)	
Taking Lamivudine	No	n%	411(100.0%)	0(0.0%)	411(80.4%)	.000*
	Yes	n%	0(0.0%)	100(100.0%)	100(19.6%)	
Total		n%	411(100.0%)	100(100.0%)	511(100.0%)	
Covid -19 Positive	No	n%	212(51.6%)	98(98.0%)	310(60.7%)	.000*
	Yes	n%	199(48.4%)	2(2.0%)	201(39.3%)	
Total		n%	411(100.0%)	100(100.0%)	511(100.0%)	

Table 2: Two by Two contingency table

| Exposure | Outcome | |
	Cases(bad)	Cases(good)
Exposed	2	98
Unexposed	199	212

Table 3: Odds ratio

Odds ratio	0.0217
95 % CI:	0.0053 to 0.0893
z statistic	5.310
Significance level	P < 0.0001

may be used probably to treat COVID-19 infection. Furthermore, there are a number of other compounds that are in development.[4] Along those lines, until more specific therapeutics become available, it is reasonable to consider more broad-spectrum antivirals that as preventive & curative options for COVID-19 infection and include Lopinavir/Ritonavir, Neuraminidase inhibitors, peptide (EK1), RNA synthesis inhibitors. It is clear however, that more research is urgently needed to identify novel chemotherapeutic drugs for treating COVID-19 infections.[4] Hence this study has been undertaken to observe whether individuals on Lamivudine are less susceptible to SARS-CoV-2 infection. Also can Lamivudine be the drug of choice for economical and effective treatment against COVID-19?

HIV-HBV co-infected patients are treated for HIV and HBV de-novo using Lamivudine (LAM), Emtricitabine (FTC) and Tenofovir (TDF) etc. With good treatment outcomes.[5] Structural similarities between SARS-CoV-2 S2 proteins and HIV-1 group 41 suggests an analogous membrane fusion mechanism[8] and that has stimulated researchers to revisit the anti-viral drug repositories used for HIV and other viruses to find a probable anti-CoV candidate.[9,10]

Combination of antiviral therapy is not new. It has been successfully used in AIDS. Improved immunologic responses associated with combination of antiretroviral therapy consisting of Zidovudine, Lamivudine and Ritonavir have been reported in AIDS patients.[11,12] Articles in literature support combination and use of re-purposive molecules as therapeutic agents for COVID-19 infection. One of the effective hepatitis C viral inhibitor 'Sofosbuvir' was found to be effective in inhibiting SARS-CoV-2 replication in lungs and brain cells and this effect was better than Remdesivir.[13] Another study demonstrated that Sofobuvir and four other nucleotide analogues (the active triphosphate forms of the HIV inhibitors Alovudine, Zidovudine, Tenofovir, Alafenamide, and Emtricitabine also inhibited the SARS-CoV-2 polymerase with different levels of efficiency.[14] Furthermore 'Sofosbuvir' and 'Velpatasvir' which together form the combination HCV drug EPCLUSA was advocated by Sayad et al[15] and Izzi et al[16] for SARS-CoV-2 treatment. Another drug 'Daclatasvir' was also shown to reduce SARS-CoV-2 induced enhancement of TNF-α and IL -6, key contribution to the cytokine storm because Velpatasvir and Daclatasvir share very similar core structures and target the same NS5A protein in HCV, and Daclatasvir has also been shown to inhibit SARS-CoV-2 replication and is currently in COVID-19 clinical trial; it is plausible that Velpatasvir and other drugs in this class, such as Ladipasvir, Elbasvir, Ombitasvir and Pibrentasvir will display similar inhibitory activity of SARS-CoV-2.[13] Also another study demonstrated that "Ramdesivir, Lopinavir, Ementine and Homoharringtonine inhibit SARS-CoV-2

replication in vitro".[17] Also Ivermectin, an FDA approved anti-parasitic previously shown to have broad-spectrum anti-viral activity in vitro is an inhibitor of SARS-CoV-2 virus.[18] The combination therapy may help to reduce the effective concentration of compounds below the therapeutic plasma concentration and provide better clinical benefits.[17] This is evident from the observations of the above findings and could be of use in COVID-19 patients.

The same is true for vaccination as well. There are currently more than 100 COVID-19 vaccine candidates under development, with a number of these in human trial phase. When a safe and effective vaccine is found, COVAX (led by WHO, GAVI and CEPI) will facilitate the equitable access and distribution of these vaccines to protect people in all countries.[19] Amidst the research and quest for development of a suitable and effective vaccine against CoV, interesting facts/findings are surfacing the scientific world. Russia had found 92% efficacy for its "Sputnik V" vaccine.[20] However that falls into various controversies amongst the scientific world. Another pharma giant, Pfizer Inc. and BioNTech SE announced their mRNA based vaccine candidate, BNT162b2, against SARS-CoV-2 with an efficacy of 90%.[21] Although various vaccines have been tried for SARS-CoV-2, recent studies showed that the measles-mumps-rubella (MMR) vaccine has been theorized to provide protection against COVID-19. It was found a statistically significant inverse correlation between mumps titre levels and COVID-19 severity in people under age 42 who have had MMR II vaccinations. This adds to other associations demonstrating that the MMR vaccine may be protective against COVID-19. The MMR II vaccine is considered a safe vaccine with very few side effects. If it has the ultimate benefit of preventing infection from COVID-19, preventing the spread of COVID-19, reducing the severity of it, or a combination of any or all of those, it is a very high reward low risk ratio intervention. Maximum sero-positivity is achieved through two vaccinations at least 28 days apart. The study also advocated that, it would be prudent to vaccinate those over 40 regardless of whether or not they already have high serum MMR titers.[22]

This may be the classical case of cross immunity or cross protection as vaccine for one virus may protect humans / may be effective against the infection of other viruses! Aren't we revisiting the history by checking various vaccines for the treatment of COVID- 19. As the vaccine initiation/history itself has its origin in cross protection. In 1798, Edward Jenner demonstrated that a person inoculated and infected with cowpox was protected against smallpox. The procedure, which he termed vaccination, represents the first use of vaccine for prevention of disease (classical cross protection example!).[23] On the similar concept it may be postulated that vaccines developed for one virus may be effective against the other as well as an antiviral molecule developed for one virus may be effective against the other

virus. This is what is observed in the present study that the individuals on anti-HBV treatment were less susceptible to SARS-CoV-2 infection. Although the findings of the present study have drawn some attention but it has some limitations that are as follows.

1. Considering the current pandemic situation, the information is collected through online or mobile phone communication. The participants are not physically / personally interviewed (Face to face).
2. Some individuals had medical history of other diseases for e.g. HTN, DM (the known co-morbidities for pathogenesis of COVID-19[6] and have taken preventive medicines like vitamin D, C, herbal preparation (Kaadha) based on the media or whatsapp group information. These factors may have contributed in the study outcomes, which was beyond the scope of this study.
3. The results of the testing information for HBV, and SARS-CoV-2 were based on oral information given by the participants.

Although limitations are their but the study results are motivating to do a research project with bigger sample size.

6. Conclusive remark

COVID-19 is an infectious disease that has asserted its presence globally and has led to a faster research activity in the field of its prevention & treatment, development of effective therapeutic agents as well as vaccines. Non availability of specific treatment and vaccines has led medical researchers to revisit the antiviral repositories, including the ones that have been used for some other viral infections like HIV, HBV etc. (re-purposive drugs). Antiviral medicine Lamivudine has been used effectively for HBV treatment and it has shown a preventive response against the SARS-CoV-2 infection. The individuals on anti-HBV treatment, taking Lamivudine are less susceptible to SARS CoV-2 infection. This might be because of some structural similarities between the coat proteins.

7. Acknowledgments

8. Conflicts of Interest

All contributing authors declare no conflicts of interest.

9. Source of Funding

References

1. Singhal T. A review of Coronavirus Disease-2019 (COVID-19) Indian. *J Paediatr*. 2020;87(4):281–6.
2. Zu ZY, Jiang MD, Xuet PP. Coronavirus disease (COVID-19), A perspective study from China. *Radiol*. 2020;296:15–25.
3. Rodrigue-Morales AJ, Cardona-Ospina JA, Gutierrez-Ocampo E. Clinical Laboratory and imaging fetaures of COVID-19: A systematic review and meta-analysis. *Travel Med Infect Dis*. 2020;34:101623.
4. Rothan HA, Byrareddy SN. The epidemiology and pathogenesis of coronavirus disease (COVID-19) outbreak. *J Autoimmu*. 2020;109:102433. doi:10.1016/j.jaut.2020.102433.
5. Maiwall R, Sarin SK, Moreau R. Asian-Pacific clinical practice guidelines on the management of hepatitis B: a 2015. *Hepatol Int*. 2016;10:1–98. doi:10.1007/s12072-015-9652-y.
6. Mousavizadeh L, Ghasemi S. Genotype and phenotype of COVID-19: Their roles in pathogenesis. *J Microbiol Immunol Infect*. 2020;doi:10.1016/j.jmii.2020.03.022.
7. Ramanna LN, Anand AR, Sethuraman S. Targeting strategies for delivery of anti-HIV drugs. *J Controlled Release*. 2014;192:271–83.
8. Zhang XW, Yap YL. Structural similarity between HIV-1 gp41 and SARS-CoV-2 S2 proteins suggests an analogous membrane fusion mechanism. *J Mol Struct*. 2004;677:73–6.
9. Michienzi SM, Badowski ME. Can vitamins and/or supplements provide hope against coronavirus? *Drugs Context*. 2020;9:5–7. doi:10.7573/dic.2020-5-7.
10. Paget J, Caini S, Cowling B, Esposito S, Falsey AR, Gentile A, et al. The impact of influenza vaccination on the COVID-19 pandemic? Evidence and lessons for public health policies. *Vaccine*. 2020;38(42):6485–6. doi:10.1016/j.vaccine.2020.08.024.
11. Lederman MM, Connick E, Landay A. Immunologic response associated with 12 weeks of combination antiretroviral therapy consisting of Zidovudine. *J Infect Dis*. 1998;178:70–9.
12. Clercq ED. New developments in anti-HIV chemotherapy. *Biochim Biophys Acta*. 2002;1587(2-3):258–75. doi:10.1016/s0925-4439(02)00089-3.
13. Jockusch S, Tao C, X L, Chien M, Kumar S, Morozova I, et al. Sofosbuvir terminated RNA is more resistant to SARS-CoV-2-2 proofreader than RNA terminated by Remdisivir. *bioRxiv*. 2020;doi:10.1101/2020.08.07.242156.
14. Jockusch S, Tao C, X L. A library of nucleotide analogues terminate RNA synthesis catalysed by polymerases of Coronaviruses that causes SARS and COVID-19. *Antiv Res*. 2020;180:104857. doi:10.1016/j.antiviral.2020.104857.
15. Sayad B, Sobhani M, Khodarahmi R. Sofosbuvir as Repurposed Antiviral Drug Against COVID-19: Why Were We Convinced to Evaluate the Drug in a Registered/Approved Clinical Trial? *Arch Med Res*. 2020;51(6):577–81. doi:10.1016/j.arcmed.2020.04.018.
16. Izzi Q, Messina V, Rinaldi L. Sofosbuvir/Velpatasvir as a combination with strong potential activity against SARS-CoV-2-2(COVID-19) infection: how to use direct-acting antivirals as broad-spectrum antiviral agents. *Eur Rev Med Pharmacol Sci*. 2020;24(10):5193–4.
17. Choy KT, Lamwong YL, Kaewpreedee P, Sia SF, Chen D, Hui KPY, et al. Remdesivir, lopinavir, emetine, and homoharringtonine inhibit SARS-CoV-2 replication in vitro. *Antiviral Res*. 2020;178:104786. doi:10.1016/j.antiviral.2020.104786.
18. Caly L, Dr'uce JD, Mg C. The FDA approved drug Ivermectin inhibits the replication of SARS-CoV-2-2 in vitro. *Antivir Res*. 2020;178:104787. doi:10.1016/j.antiviral.2020.104787.
19. The push for COVID-19 vaccine; accessed on 02-12-2020. Available from: www.who.int.
20. J Cohen, Science Nov 11 2020 www.ScienceMag.org. Accessed on 02-12-2020;.
21. www.pfizer.com/press release detail. https://www.businesswire.com/home/20201109005539/en/.Accessd on 02-12-2020.
22. Gold JE, Baumgaryl WH, Okay RA. Analysis of Measles-Mumps-Rubella (MMR) titres of recovered COVID-19 patients. *mBio*. 2020;11(6):2628–48.
23. Sjögren MH, Cheatham JG. Chapter 21 - Hepatitis Vaccines and Immunoprophylaxis, Editor(s): Peter R. McNally,GI/Liver Secrets. In: McNally PR, editor. GI/Liver Secrets 4th Edn. 10.1016/B978-0-323-06397-5.00021-6: Mosby; 2010. p. 151–7.

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