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CONNEXION OF SUN LIGHT EXPOSURE, USE OF PHOTOSENSITIZING SUBSTANCES AND SUBJECT'S PRACTICES, WITH THE DEVELOPMENT AND SEVERITY OF COVID-19 DISEASE

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ABSTRACT

Back ground &Objective: Concerning the prevention and management of corona virus disease, many modalities have been in trial. Effect of sun light and related themes are also under discussion in this regard with no definite proof. With the same intention we have combined the three parameters in our research so to observe the correlation of sun light exposure, use of photosensitizing substances and subject's practices with the development and severity of covid-19 disease. Materials and methods: Covid-19 PCR positive patients were included in the study as cases, while gender matched house mate as controls. Study subjects were divided in two groups. In group 1 cases were diseased while controls were not diseased. In group 2 cases were having more symptoms and control with less symptoms. Results: Male Gender, higher education and being married affected the occurrence of disease while older age affected both the occurrence and severity. Good Sun exposure at work place was more seen in the controls of disease occurrence while direct sun exposure per week >100 minute was more frequent in the controls of both groups. DM (Diabetes Mellitus) was more common in cases of disease occurrence group while HTN (hypertension) was more common in cases of disease severity group. OAD (obstructive airway disease) was seen more in controls of disease occurrence group. Use of ACEi (angiotensin converting enzyme inhibitor) was more common in cases of disease occurrence group while use of ARB (angiotensin receptor blocker) was found more common in cases of disease severity group. Intercity travel, and history of attending the gathering was more in cases of disease occurrence group. Conclusion: Sun exposure prevented the disease occurrence and severity, OAD prevented the disease occurrence, DM, ACEi, gatherings and intercity travels were related to disease occurrence, HTN and ARB were related to disease severity.

KEYWORDS: corona disease occurrence, corona disease severity, role of sun light in corona.

INTRODUCTION

The Covid-19, a disease related to novel corona virus, has become a name of dread since December 2019, when Wuhan city of china was first noticed for the novel corona virus cases with an expected epidemic. [1] Then soon after, the fire caught the whole world, more than 200 countries of the world got involved in the knots of covid 19 within two months after the epidemic started.

Different theories has been proposed until now including conspiracies regarding the onset of this pandemic and this is however well believed that this virus family belongs to family of bats. Bats have been recognized as the natural reservoirs of a large variety of viruses. [2] Many factors has been described as contributory regarding the spread and prevention of this disease, among which behaviours play a very important role like

seriousness and compliance of covid preventive protocols; like hand washing, social distancing, use of face mask etc.^[3]

Since this was a novel and un-expected outbreak so still we are waiting for the ultimate and straight forward cure of corona virus disease to come up. Many drugs have been tried recently in the treatment for covid-19^[4] and further research is going on regarding preparation of vaccines, Intravenous Immuno-globulins, plasma of recovered patient, antiviral therapy, and other modalities.

Currently there is great debate on the antiviral properties of different substances. There are certain studies which displayed that photosensitization, natural (phytochemicals) or synthetic can be effective (preventive) against certain viral diseases, of which

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certain components we are naturally exposed to, for example, sun light itself, chlorophyll (green leafy vegetables), turmeric, lemon and other citrus fruits etc. ^[5]

So we planned this study to see whether this correlation between the subject's practices, social behaviors, sun light exposures, use of photosensitizing substances, and development of COVID-19 disease and its severity exists or not, and which of the above mentioned factors is more dominant, to further add on disease preventive and management strategies.

MATERIALS AND METHODS

All PCR positive patients of covid -19, from in and out department of Shifa International hospital and Shifa Falahee clinics (Islamabad, Pakistan) during the month of March to August 2020, were included in the study as cases, and their gender matched house mate as controls. Patients who were not willing, or without controls, were excluded from the study. All the study subjects were divided in two groups. Group 1 was based on disease occurrence with the cases having disease while controls were not diseased, group 2 was based on severity with the cases having more severe symptoms and control with less severe symptoms. Performa distributed to both groups were same and included questions about demographic characteristics, comorbid conditions, use of any of the drugs (photosensitizing drugs); ACE i, ARB, statins, NSAIDS(non-steroidal anti-inflammatory drugs), SSRI (selective serotonin reuptake inhibitor), phenothiazine, Amiodarone, tetracycline, sulphonylurea, anti-histamines; use of common photosensitizing dietary substances like lemon, citrus fruits, green leafy vegetables, turmeric; preventive practices; travel history; sun light exposure per week at and at work place. SPSS 23 was used for data entry. Descriptive stats were calculated for both qualitative and quantitative data. For qualitative data, percentages, while for quantitative data; mean, standard deviation were calculated. Effect modifiers like gender, age, comorbid, drug history,

marital status, sun exposures, covid exposure, and travel history were controlled through stratification and post stratification, Chi square or Fischer's exact were calculated and p value < 0.05 with 95% confidence interval was considered statistically significant.

RESULTS

Total 450 subjects (158 cases and equal controls for Group 1, 67 cases and equal controls for Group 2) were enrolled.

In disease occurrence group, most of cases were (98 out of 152) in range of 40-80 years, while most of controls were in range of 20-40years (74 out of 128) (p=0.000). Mean age of this group was 40.54 with SD±17.88. Out of 316 subjects, 214 were male and 102 were female. Among 316 subjects, 108 were single, 206 were married and 2 were widowed. Most of the single (74%) belonged to control group and most of married (60.2%) belonged to cases (p=0.000). Education level graduation and above was more prevalent among cases (103 out of 174) while below graduation was more prevalent among controls (80 out of 128) (p= 0.001). Among 264 who did not travel, majority (53.4%) were controls, while 51 who travelled intercity majority (66.7%) were cases. (p=0.002). (Table 1)

Table 1: Summary of effect of variables on cases and controls in Group 1 (Disease occurrence group) and Group 2 (Disease severity group)

Sr/no	Variable	Group 1		P value	Group 2		P value
		n=316			n= 134		
		Case	control		Case	Control	
1	Age:						
	<40 years	60(164)	104(164)	0.000	29(72)	43(72)	0.017
	40-80	97(141)	54(141)		38(61)	23(61)	
2	Gender:						
	Male	107(214)	107(214)	0.074	34(68)	34(68)	0.56
	Female	51(102)	51(102)		33(66)	33(66)	
3	Marital status:						
	Single	34(108)	74(108)	0.000	18(45)	27(45)	0.62
	Married	124(106)	82(106)		49(87)	38(87)	
	Widowed	0(2)	2(2)		0(2)	2(2)	
4	Education:						
	Graduate &above	103(174)	71(174)	0.001	43(84)	41(84)	0.664
	Below graduate	48(128)	80(128)		20(36)	16(36)	
	Illiterate	7(14)	7(14)		8(14)	6(14)	

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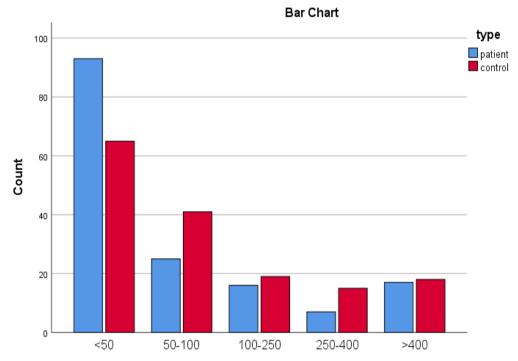
5	Out city Travel:						
	None	123(264)	141(264)	0.002	57(114)	57(114)	0.595
	Intercity	35(52)	17(52)	0.002	10(20)	10(20)	0.333
6	Covid19	33(32)	17(32)		10(20)	10(20)	
0	Exposure:						
	Yes	46(88)	42(88)	0.707	26(54)	28(54)	0.43
	No	112(227)	115(227)	0.707	41(80)	39(80)	0.43
7	Sunny condition at	112(221)	113(221)		41(60)	39(00)	
/	Work place:						
	Good	121(256)	135(256)	0.031	50(100)	50(100)	0.57
	Bad	37(60)	23(60)	0.031	17(34)	17(34)	0.57
8	Sun Exposure per	37(00)	23(00)		17(34)	17(34)	
0	week:						
	<100 min	118(224)	106(224)	0.004	50(96)	46(96)	0.027
9	>100 min >100mins	40(92)	52(92)	0.004	34(75)	41(75)	0.027
	Co-Morbid:	40(32)	32(92)		34(73)	41(73)	
9	DM	119(122)	3(122)	0.000	2(3)	1(3)	0.003
	HTN	39(179)	3(122) 140(179)	0.000	2(3) 8(8)	1(3) 0(8)	0.003
	OAD	0(13)	13(13)		1(2)	1(2)	
10	ACE Inhibitors:	0(13)	13(13)		1(2)	1(2)	
10	Yes	13(19)	6(19)	0.077	0(3)	3(3)	0.24
	No	145(297)	152(297)	0.077	67(131)	64(131)	0.24
11	ARB Use:	143(291)	132(291)		07(131)	04(131)	
11	Yes	12(20)	8(20)	0.245	6(7)	1(7)	0.058
	No	146(296)	150(296)	0.243	61(127)	66(127)	0.038
13	Statin Use:	140(290)	130(290)		01(127)	00(127)	
13	Yes	9(11)	2(11)	0.032	4(8)	4(8)	1.0
	No	149(305)	156(305)	0.032	63(134)	63(134)	1.0
14	Lemon Use:	149(303)	130(303)		03(134)	03(134)	
14	Yes	124(258)	134(258)	0.34	52(108)	56(108)	0.693
	No	34(58)	24(58)	0.34	15(26)	11(26)	0.093
15	Citrus Intake:	34(30)	24(30)		13(20)	11(20)	
13	Yes	135(278)	143(278)	0.293	53(108)	55(108)	0.903
	No	23(38)	15(38)	0.293	14(26)	12(26)	0.903
16	Turmeric Use:	23(30)	13(36)		14(20)	12(20)	
10	Yes	140(277)	137(277)	0.163	52(107)	55(107)	0.727
	No	18(39)	21(39)	0.103	15(25)	12(25)	0.727
17	Green Leafy Veg	10(37)	21(3))		13(23)	12(23)	
1 /	Yes	139(287)	148(287)	0.217	65(130)	65(130)	1.00
	No	19(29)	10(29)	0.217	2(4)	2(4)	1.00
18	Preventive	17(27)	10(27)		2(1)	2(1)	
10	Practice:						
	Best	53(101)	48(101)	0.667	24(50)	26(50)	0.8
	Average	76(160)	84(160)	0.007	31(63)	32(63)	0.0
	None	29(55)	26(55)		12(21)	9(21)	
19	Attended	=>(55)	_==(==)		1-(21)	/(21)	
-/	Gathering 2 weeks						
	before:						
	Yes	30(50)	20(50)	0.082	20(39)	19(39)	0.5
	No	128(266)	138(266)	3.002	47(95)	48(95)	0.0
20	Frequency of Out	120(200)	150(200)		17(55)	10(33)	
20	Visits:						
ı	Daily	77(147)	70(147)	0.72	16(25)	19(25)	0.578
	2-3times/week	55(110)	61(116)	3.72	39(79)	40(79)	0.270
	None 2 Stimes/ week	26(53)	27(53)		12(20)	8(20)	
	1,0110	20(33)	27(33)	<u> </u>	12(20)	0(20)	

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ACE, angiotensin converting enzyme; ARB, angiotensin receptor blocker

Among 256 good sunny workplace conditions, majority (52.7%) were retained by controls and among 60 bad sunny workplace conditions majority (61.7%) were possessed by cases (p=0.031).

Among 224 who had direct sun exposure <100 minutes per week, majority, 118(224) belonged to cases in comparison to 106(224) controls. Among 92 who had direct sun exposure >100 minutes /week, majority 52(92) belonged to controls and rest 40(92) belonged to cases. (Figure 1)



Sun exposure/week (in minutes)

Figure 1: direct sun exposure per week in minutes among cases and controls in disease occurrence group (Group 1).

Among comorbid conditions, 179 subjects had HTN and majority (140) were control, 122 had DM and majority (119) were cases, 13 had OAD (either COPD or asthma, were not further sorted out) and all were controls. (p=0.000) (Table 1)

Only 19 were using ACEi and majority (13(68.4%)) were cases, 20 were using ARB's and among them majority (12 (60%)) were cases. (p=0.07, 0.245 respectively). Among 11 statin users, 9(81.8%) were cases (p=0.032) (Table 1)

Lemon and other citrus fruit intake, use of green leafy vegetables, use of turmeric was statistically same among cases and controls (p=0.34, 0.34, 0.29, 0.21 respectively). (Table 1)

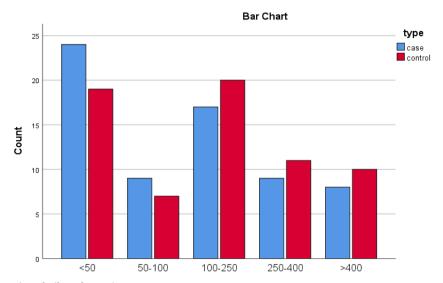
Preventive practices were also statistically not different among cases and controls (p=0.667) while among 50 subjects who attended gatherings in 2 weeks prior to onset of symptoms, 30(60%) were cases with borderline

statistical significance (p= 0.082), otherwise as a whole frequency of going outside were statistically not different in cases and controls (p=0.72) (Table 1)

In disease severity group, following observations were made. 68 (out of 134) were males, 66 (out of 134) were females. Among 45 who were single, majority (60%) were controls and among 87 married, 56.3% were cases (p=0.62). Among 72 who were below 40 years of age, 43 belonged to control group, while from 40-80 year age group,38 subjects out of 54 belonged to cases (p=0.000). Mean age of this group was 39.77 with SD±17.88. (Table 1)

Education, travel history, covid 19 exposure, sun exposure at work place, were statistically not different among cases and controls.(Table 1) However 33 out of 59 who had sun exposure <100 minutes per week, were cases, while among 75, 41 had sun exposure more than 100 minutes, belonged to controls (p=0.027). (Figure 2)

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Sun exposure/week (in minutes)

Figure 2: Direct sun exposure per week in minutes among cases and controls in disease severity group (Group 2)

Among 134 subjects, only 16 subjects had associated comorbid conditions. Diabetic were only 3 and hypertensive were 8 and all belonged to cases group (p=0.003) while OAD cases were very few (2) and same in cases and controls (Table 1).

Among 7 who were ARB users, 6 belonged to cases(p=0.058), while use of ACEi, lemon and other citrus, green vegetables, turmeric, preventive practices, attending gathering in last 2 weeks and frequency of out visits were not statistically different among cases and controls. (Table 1)

DISCUSSION

Though the scuffles against corona virus has stretched up to the vaccinations at mass level, but effect of vaccination is estimated to be limited in time (few months) and antibody production response may differ from person to person, so the preventive measures may remain standard of care in this pandemic. We need to continue reviewing the factors which can help in corona prevention and severity reduction, so the need for further research is inevitable. ^[6]

Our study results showed males were more prone to develop covid-19 disease but severity was not affected by the gender. Gender effect on occurrence and mortality of covid-19 disease is a matter of concern for other researchers also^[7] and this might unveil the effect of sex hormone in disease occurrence and severity.

Age affected the disease occurrence and severity both in our study in that age above 40 was more associated with disease occurrence and severity. This age multitude is an already research proven fact in many articles. [8, 9]

Being single in our study seems to be correlated with disease prevention but we should remember that less disease occurrence in under 40 years of age group is colluding with single status which is prevalent under same age group.

Interestingly, education impacted negatively on the occurrence of corona virus disease but not the severity. Indoor employment which is tied to more literacy level in our society, stressful jobs, junk diets at office, and small accommodations with compromised sunny and ventilation conditions in private sector might explain all this.

Most common comorbid conditions in our study was HTN then DM. As many of the literature stated the same finding that most common pre-existing comorbidities are hypertension and diabetes. [9, 10, 11, 12] We further observed the DM is more prone to disease occurrence, however once diseased, HTN is more susceptible to develop more severe disease. In a large case series from China; they found an overall case fatality rate increased for people with hypertension. [13] A study-level meta-analysis of 2552 confirmed COVID-19 patients reported a pooled odds ratio (OR) of 2.49 for severe disease in the presence of hypertension, with low heterogeneity between studies. Weak evidence from meta-regression suggested that hypertension might be a clinical predictor of COVID-19 severity in people aged over 60.[14] Likewise, a retrospective cohort analysis in China confirmed apparent high mortality in patients presenting with hypertension. [15] These data suggested that COVID-19 patients with hypertension tended to show more severe inflammation and organ damage than COVID-19 patients without hypertension. [16]

Eva L et al has stated that COVID-19 has collided with diabetes, creating especially susceptible populations of patients with both COVID-19 and diabetes. [17] As COVID-19 lacks definitive treatment so far, the susceptibility finding of diabetes mellitus is important in that to endorse diabetics to follow general preventive

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rules more strictly and monitor glucose levels more frequently. [18]

Our study results revealed protective effect of OAD against occurrence of covid-19 disease, it was astounding for us as well but Carli G and colleagues well hypothesized the mechanism of possible protective effect of Asthma against development of covid-19 disease. Our study results endorsed their findings. [18b]

We also found ACEi users more prone to develop disease, while ARB users to develop more severe disease symptoms. ACEi use could act as a marker of increased mortality risk in some but not all COVID-19 disease settings, says Nunes JPL et al. [19] Although some animal studies suggested that their use could have value in preventing and treating the effects of the COVID-19, there are also contradictory scenarios suggesting that the use of ACEIs/ARBs may exacerbate the deleterious conditions of the infection. Either they are useful or harmful for covid-19, might have been displayed under specific physical conditions which are not yet known. So this is still an area requiring exploration. [20]

Our study proclaimed the effect of sun more strongly depicting its effect in prevention of disease occurrence and its severity. There are certain studies which demonstrated the effect of UV radiations (ultra violet, component of sun light) on this virus. Ahmadi M et al concluded in their study that significantly negative correlations were found between COVID-19 infection rate and UV radiation in all cities with available UV data (5 out of 9 analyzed cities); they further stressed that the sensitivity analysis pointed out UV radiation as a significant variable. [21] More importantly, Sagripanti and Lytle have recently predicted the inactivation of SARS-CoV-2 by solar UVB in densely populated cities in the world .The authors have estimated that during the winter season in the city of São Paulo, a 41-min exposure to sunlight around solar noon would be required to achieve 90% inactivation of SARS-CoV-2 virus, while a 13-min exposure to sunlight around solar noon could achieve 99% inactivation during the summer season. Findings from some other studies have also reinforced that UV radiation provided by sunlight potentially reduces the infectivity of SARS-CoV-2. [22, 23] So provision of good sunny conditions at work place and direct sun exposure should be fetched into practice to deal with the occurrence and severity of corona virus disease.

Almeida A has further proposed that if not UV light, the use of photodynamic therapy (PDT) can be an alternative approach against SARS-CoV-2 that deserves to be explored. PDT requires the use of a photosensitizer (PS), a molecule that, after being excited by visible light produces photodynamic effect on the body. [24]

Regarding the use of lemon, turmeric, green leafy vegetables and drugs as photosensitizing substances(Phenothiazine, SSRI's NSAID's, Anti-

histamine, Statins, Amiodarone, sulfonylurea) information remained vague and most of study subjects were themselves never noticed their dietary facts exactly and the photosensitizing drugs we asked about, most of them were not aware of their generics, so exact information could not be gathered. We here do recommend quantifiable dietary and drug information that should be gathered in larger and focused trials to exactly find out the matter of these substances with the occurrence and severity of covid-19disease.

As other case control studies, recall bias remains the most important weakness of the study particularly about diet and drugs, however the sun exposure related findings of our study are less likely to be affected by recall and should be taken seriously and "sun related" preventive and management options should be taken into consideration by the researchers. Our study highlights the importance of sun exposure but the preventive effect of photosensitizing substances could not expound. Nevertheless, use of sun light component (UV radiations, infra-red or any other) in prevention and management of corona virus disease has exponential need of exploration.

CONCLUSION

Age below 40, prevented the disease occurrence and severity, female gender, being single and lower literacy level prevented the disease occurrence. Sunny work place conditions and direct sun exposure prevented the disease occurrence and severity both, DM and ACEi were related to disease occurrence, HTN and ARB were related to disease severity. OAD prevented the disease occurrence while gatherings and intercity travels were related to disease occurrence.

CONFLICT OF INTEREST: None.

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