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Original article

Binary Logistic Regression Analysis of the Relationship Between Lunar Month of Diagnosis of Autoimmune Hepatitis and Treatment Options

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Abstract

Immunosuppressive has been the main treatment for patients with moderate or severe autoimmune hepatitis (AIH) as the survival benefits have clearly been demonstrated in clinical trials. Seasonal variations in treatment have not been studied yet, hence, we aim to study the potential relationship between the Lunar month of diagnosis and treatment options in AIH. All cases of AIH who presented to our hospitals between Jan 2016 and Jan 2021 were reviewed. Data was analyzed using the binary logistic regression model and Chi-square test of association to establish any potential relationship between the Lunar month of diagnosis and treatment response in AIH. Total number of patients with clinically and histologically proven AIH was sixty. Forty-seven were females (78.33%) and 28.33% were males (n=17). Liver biopsies were recorded in twenty-six cases (43.3%) among whom, interface hepatitis was found in ten patients (16.7%).

Total of twelve patients were not on any treatment and five of them (41.6%) had been diagnosed during the Full Moon (FM) phase. Patients who have been diagnosed with AIH during the Third Quarter (TQ) Phase were only three (5.0%), however 66.6% of them were on combination therapy of Steroids and Azathioprine (AZA). Interestingly, fifth of the patients were diagnosed during the First Quarter phase and only one of them were on combined therapy.

Ten patients in total were on steroids only among whom 40% were diagnosed during the FM phase. The Chi-square test of association showed a non-significant association of the lunar month of diagnosis with the treatment they receive, X^2 (9, N= 31) = 7.99, p = .535.

Steroids and AZA treatment exhibited lower frequency on full moon and third quarter moon than new and first quarter moon. Our data show that patients diagnosed with AIH during the FM phase of the lunar cycle are less likely to require combination therapy of steroids and AZA. We could not establish any significant relation between the lunar month of diagnosis and treatment response in AIH.

Keywords: ***Autoimmune Hepatitis; Immunosuppression in Liver Disease.***

Introduction

New moon (NM), first quarter (FQ), full moon (FM), and third quarter (TQ) of the lunar month have varying gravitational pulls on the earth [1,2]. The amplitude of ocean tidal currents varies as per the relative location of the moon in its orbit, demonstrating this fluctuation in lunar gravitational force [1,3,4]. The moon's gravitational pull could have an impact on the human body's fluid compartments [1]. The human body contains around 42 liters of water (60 percent of body weight) [5] and, like sea water, the body water may form some type of tidal wave, which has been dubbed "human tidal wave" or "biological tide" [1,6]. The idea of "biological tide" was utilised by these authors to describe the moon effect on human emotional disturbance. Though there is much debate concerning the impact of lunar rhythm on human behaviour and illness onset [7-10], the fundamental concerns about lunar rhythm's influence on physiological systems remain unsolved. The lunar cycle has been attributed with the power to influence a variety of human phenomena across history. Nonetheless, proof supporting the moon's alleged impact on human behaviour has proven difficult, and research has tended to suffer from methodological and data analysis flaws. We reviewed Medline, PubMed, and the bibliographies of similar papers and were unable to find any research that examined the lunar fluctuation and its impacts on areas of human life such as, relationship of lunar month of diagnosis with gender, month of birth, symptoms of presentations, ALP/AST ratio, treatment they receive, other autoimmune diseases, special moon events, relationship of lunar month of diagnosis with cirrhosis, and relationship of special moon events with cirrhosis.

Material and methods

Study design and setting

A prospective cohort study was used to assess the relation of Lunar Month of Diagnosis with clinical and sociodemographic characteristics including Month of Birth, Gender, Histological

findings Symptoms of Presentation, nature of Treatment patient is on (AzA: azathioprine, steroids etc.), Development of ALF (Acute Liver failure), Association with other Autoimmune Disease.

Data analysis

Microsoft Excel was used for data management (Microsoft Office, Redmond, Washington, United States) and statistical analysis was performed by using statistical package for social sciences (SPSS v26) and Jamovi (v 2.2.3). The categorical data were presented as frequency and percentage while the continuous data were presented as a mean and standard deviation. The binary logistic regression model was implied to assess the association association of Special Moon event with Cirrhosis a Chi-square test of association was run. The P-value was stated significant if ≤ 0.5.

Results

To explore the association of Lunar Month of Diagnosis with clinical and sociodemographic characteristics including Month of Birth, Gender, Histological findings Symptoms of Presentation, nature of Treatment patient is on (AzA: azathioprine, steroids etc.), Development of ALF (Acute Liver failure), Association with other Autoimmune Disease, Special Moon event, and Cirrhosis a series of Chi-square test of Association were run using Jamovi. Further to examine the association of Special Moon event with Cirrhosis a Chi-square test of association was run. Table 1 to 9 shows the detail results of Chi-square test of association.

Furthermore, to explore the clinical characteristics including Liver Biopsy, DEXA Scan, Histological findings, Treatment they on, level of serum globulin and the history of ANA positive of the patients with Autoimmune Hepatitis reviewed in the hospital over the last 5 years, descriptive statistics were run using Jamovi. Table 10 and Figure 1-8 shows the details.

Table 1: Relationship of Lunar Month of Diagnosis with Gender.

		Sex		
Lunar Month of Diagnosis		**Female**	**Male**	**Total**
New Moon	Observed	4	4	8
	Expected	5.68	2.323	8.00
First Quarter	Observed	7	3	10
	Expected	7.10	2.903	10.00
Full Moon	Observed	9	1	10
	Expected	7.10	2.903	10.00
Third Quarter	Observed	2	1	3
	Expected	2.13	0.871	3.00
Total	Observed	22	9	31
	Expected	22.00	9.000	31.00

A Chi-square test of Association was performed to examine the relationship of Lunar Month of Diagnosis with Gender. The Chi-square test of association showed a non-significant association of Lunar Month of Diagnosis with Gender, X^2 (3, N= 31) = 3.50, p = .321. Further, the findings showed that despite the non-significant Chi-square test of association, the male exhibited higher frequency on new moon than female. However, male exhibited lower frequency on full moon than female.

Table 2: ***Relationship of Lunar Month of Diagnosis with Month of Birth***

		Lunar Month of Diagnosis				
Month of Birth		**New Moon**	**First Quarter**	**Full Moon**	**Third Quarter**	**Total**
December	Observed	1	2	1	1	5
	Expected	1.290	1.613	1.613	0.484	5.00
October	Observed	0	0	2	1	3
	Expected	0.774	0.968	0.968	0.290	3.00
March	Observed	0	2	0	0	2
	Expected	0.516	0.645	0.645	0.194	2.00
August	Observed	2	0	0	0	2
	Expected	0.516	0.645	0.645	0.194	2.00
July	Observed	1	0	1	0	2
	Expected	0.516	0.645	0.645	0.194	2.00
September	Observed	2	1	1	0	4
	Expected	1.032	1.290	1.290	0.387	4.00
January	Observed	1	0	2	0	3
	Expected	0.774	0.968	0.968	0.290	3.00
April	Observed	0	2	0	0	2
	Expected	0.516	0.645	0.645	0.194	2.00
February	Observed	0	2	0	0	2
	Expected	0.516	0.645	0.645	0.194	2.00
June	Observed	1	1	0	0	2
	Expected	0.516	0.645	0.645	0.194	2.00
May	Observed	0	0	3	1	4
	Expected	1.032	1.290	1.290	0.387	4.00
Total	Observed	8	10	10	3	31
	Expected	8.000	10.000	10.000	3.000	31.00

A Chi-square test of Association was performed to examine the relationship of Lunar Month of Diagnosis with Month of Birth. The Chi-square test of association showed a non-significant association of Lunar Month of Diagnosis with Month of Birth, X^2 (30, N= 31) = 36.30, p = .200.

Table 3: ***Relationship of Lunar Month of Diagnosis with Symptoms***

		Lunar Month of Diagnosis				
Symptoms		**New Moon**	**First Quarter**	**Full Moon**	**Third Quarter**	**Total**
No Symptoms	Observed	4	6	7	0	17
	Expected	4.387	5.484	5.484	1.6452	17.00
Abdominal Pain	Observed	1	2	0	0	3
	Expected	0.774	0.968	0.968	0.2903	3.00
Loss of Appetite	Observed	1	0	0	1	2
	Expected	0.516	0.645	0.645	0.1935	2.00
Dark Urine	Observed	1	0	1	0	2
	Expected	0.516	0.645	0.645	0.1935	2.00
Jaundice	Observed	1	0	1	1	3
	Expected	0.774	0.968	0.968	0.2903	3.00
ALF	Observed	0	1	1	1	3
	Expected	0.774	0.968	0.968	0.2903	3.00
Vomiting	Observed	0	1	0	0	1
	Expected	0.258	0.323	0.323	0.0968	1.00
Total	Observed	8	10	10	3	31
	Expected	8.000	10.000	10.000	3.0000	31.00

A Chi-square test of Association was performed to examine the relationship of Lunar Month of Diagnosis with Symptoms of presentations. The Chi-square test of association showed a non-significant association of Lunar Month of Diagnosis with Symptoms of presentations, X^2 (18, N= 31) = 18.50, p = .420. Further, the findings showed that despite the non-significant Chi-square test of association, the No symptoms exhibited higher frequency on full moon than new, first quarter and third quarter moon.

Table 4: Relationship of Lunar Month of Diagnosis with *ALPAST* or *ALT Ratio*

		ALPAST or ALT Ratio			
Lunar Month of Diagnosis		**<1.5**	**1.5-3.0**	**>3.0**	**Total**
New Moon	Observed	5	0	3	8
	Expected	4.13	1.290	2.581	8.00
First Quarter	Observed	4	3	3	10
	Expected	5.16	1.613	3.226	10.00
Full Moon	Observed	5	2	3	10
	Expected	5.16	1.613	3.226	10.00
Third Quarter	Observed	2	0	1	3
	Expected	1.55	0.484	0.968	3.00
Total	Observed	16	5	10	31
	Expected	16.00	5.000	10.000	31.00

A Chi-square test of Association was performed to examine the relationship of Lunar Month of Diagnosis with ALPAST or ALT Ratio. The Chi-square test of association showed a non-significant association of Lunar Month of Diagnosis with ALPAST or ALT Ratio, X^2 (6, N= 31) = 3.74, p = .711. Further, the findings showed that despite the non-significant Chi-square test of association, the 1.5-3.0 range of ALPAST or ALT Ratio exhibited lower frequency on new moon than full, first quarter and third quarter moon.

Table 5: ***Relationship of Lunar Month of Diagnosis with Treatment they Receive***

		Lunar Month of Diagnosis				
Treatment		**New Moon**	**First Quarter**	**Full Moon**	**Third Quarter**	**Total**
No treatment	Observed	3	3	5	1	12
	Expected	3.097	3.871	3.871	1.161	12.00
Steroids	Observed	3	3	4	0	10
	Expected	2.581	3.226	3.226	0.968	10.00
AZA	Observed	0	1	1	0	2
	Expected	0.516	0.645	0.645	0.194	2.00
Steroids and AZA	Observed	2	3	0	2	7
	Expected	1.806	2.258	2.258	0.677	7.00
Total	Observed	8	10	10	3	31
	Expected	8.000	10.000	10.000	3.000	31.00

A Chi-square test of Association was performed to examine the relationship of Lunar Month of Diagnosis with Treatment they receive. The Chi-square test of association showed a non-significant association of Lunar Month of Diagnosis with Treatment they Receive, X^2 (9, N= 31) = 7.99, p = .535. Further, the findings showed that despite the non-significant Chi-square test of association, the Steroids and AZA treatment exhibited lower frequency on full moon and third quarter moon than new and first quarter moon.

Table 6: Relationship of Lunar Month of Diagnosis with Other Autoimmune Diseases

		Lunar Month of Diagnosis				
Other Autoimmune Diseases		**New Moon**	**First Quarter**	**Full Moon**	**Third Quarter**	**Total**
No	Observed	4	6	7	2	19
	Expected	4.90	6.13	6.13	1.84	19.0
Yes	Observed	4	4	3	1	12
	Expected	3.10	3.87	3.87	1.16	12.0
Total	Observed	8	10	10	3	31
	Expected	8.00	10.00	10.00	3.00	31.0

A Chi-square test of Association was performed to examine the relationship of Lunar Month of Diagnosis with Other Autoimmune Diseases. The Chi-square test of association showed a non-significant association of Lunar Month of Diagnosis with Other Autoimmune Diseases, X^2 (3, N= 31) = 0.79, p = .851.

Table 7: Relationship of Lunar Month of Diagnosis with Special Moon Events

		Lunar Month of Diagnosis				
Special Moon Events		**New Moon**	**First Quarter**	**Full Moon**	**Third Quarter**	**Total**
Micro Full Moon	Observed	1	1	3	0	5
	Expected	1.364	1.364	2.045	0.2273	5.00
Total lunar eclipse	Observed	0	0	1	0	1
	Expected	0.273	0.273	0.409	0.0455	1.00
Super New Moon	Observed	4	1	0	0	5
	Expected	1.364	1.364	2.045	0.2273	5.00
Super Full Moon	Observed	1	2	2	0	5
	Expected	1.364	1.364	2.045	0.2273	5.00
Partial Lunar Eclipse	Observed	0	1	0	1	2
	Expected	0.545	0.545	0.818	0.0909	2.00
Black Moon	Observed	0	1	1	0	2
	Expected	0.545	0.545	0.818	0.0909	2.00
Blue Moon	Observed	0	0	2	0	2
	Expected	0.545	0.545	0.818	0.0909	2.00
Total	Observed	6	6	9	1	22
	Expected	6.000	6.000	9.000	1.0000	22.00

A Chi-square test of Association was performed to examine the relationship of Lunar Month of Diagnosis with Special Moon Events. The Chi-square test of association showed a non-significant association of Lunar Month of Diagnosis with Special Moon Events, X^2 (18, N= 22) = 25.20, p = .120. Further, the findings showed that despite the non-significant Chi-square test of association, the super new moon exhibited higher frequency on new moon than new, first quarter and third quarter moon.

Table 8: Relationship of Lunar Month of Diagnosis with Cirrhosis

		Lunar Month of Diagnosis				
Cirrhosis		**New Moon**	**First Quarter**	**Full Moon**	**Third Quarter**	**Total**
No	Observed	7	4	7	0	18
	Expected	4.65	5.81	5.81	1.74	18.0
Yes	Observed	1	6	3	3	13
	Expected	3.35	4.19	4.19	1.26	13.0
Total	Observed	8	10	10	3	31
	Expected	8.00	10.00	10.00	3.00	31.0

A Chi-square test of Association was performed to examine the relationship of Lunar Month of Diagnosis with Cirrhosis. The Chi-square test of association showed a significant association of Lunar Month of Diagnosis with Cirrhosis, X^2 (3, N= 31) = 8.93, p = .030. Further, the findings showed that having cirrhosis exhibited higher frequency on the first quarter and third quarter moon than new moon and full moon.

Table 9: Relationship of Special Moon Events with Cirrhosis

		Cirrhosis		
Special Moon Events		**No**	**Yes**	**Total**
Micro Full Moon	Observed	4	1	5
	Expected	2.955	2.045	5.00
Total Lunar Eclipse	Observed	0	1	1
	Expected	0.591	0.409	1.00
Super New Moon	Observed	3	2	5
	Expected	2.955	2.045	5.00
Super Full Moon	Observed	2	3	5
	Expected	2.955	2.045	5.00
Partial Lunar Eclipse	Observed	1	1	2
	Expected	1.182	0.818	2.00

Black Moon	Observed	1	1	2
	Expected	1.182	0.818	2.00
Blue Moon	Observed	2	0	2
	Expected	1.182	0.818	2.00
Total	Observed	13	9	22
	Expected	13.000	9.000	22.00

A Chi-square test of Association was performed to examine the relationship of Special Moon Events with Cirrhosis. The Chi-square test of association showed a non-significant association of Special Moon Events with Cirrhosis, X^2 (6, N= 22) = 4.63, p = .593. Further, the findings showed that having cirrhosis exhibited higher frequency on the first quarter and third quarter moon than new moon and full moon.

Table 10: Clinical Characteristics of the Study Population (n = 61)

Variable	**Category**	***f***	***%***
Liver Biopsy			
	Yes	26	43.3
	No	34	56.7
Liver Histology			
	Predominantly Lymphoplasmacytic Infiltrate	2	3.3
	Interface Hepatitis	10	16.7
	Active Inflammation and Cirrhosis	1	1.7
	Atypical Features	1	1.7
	No Record	12	20.0
	None of the above	34	56.7
Alcohol Intake			
	< 25g/day	34	56.7
	25-60g/day	1	1.7
	>60g/day	3	5.0
	Non-alcohol	9	15.0
	No Record	13	21.7
Hepatitis Viral Marker			
	Positive	3	5.0
	Negative	46	76.7
	Not Done	11	18.3
AMA Positive			
	Yes	2	3.3
	No	50	83.3
	Not Done	8	13.3
Vaccination			
	HAV	5	8.3
	HBV	4	6.7
	HAV & HBV	3	5.0
	Not Vaccinated	48	80.0
DEXA			
	Yes	17	28.3
	No	33	51.0
	Not Done	10	16.7
Serum Globulin			
	<1	14	25.9
	1-1.5	7	13.0
	1.5-2.0	12	22.2
	>2.0	7	13.0
	No test	14	25.9

Table 10 shows the descriptive statistics of clinical characteristics for the study population. The findings indicated that about 43% of the sample had liver biopsy. Further the findings indicated that only 17% had Interface Hepatitis while majority had no liver histology (57%) followed by those had no record (20%). Furthermore, the results indicated that majority (57%) had a history of alcohol intake less than 25g/day, followed by greater than 60g/day (5%). However, 22% had no history followed by patients had not taking alcohol (15%). In terms of Hepatitis viral marker, only 5% cases had a history of Positive while majority (77%) had negative history followed by 18% who had no record. Further the results indicated that only 3% had a AMA positive and majority (83%) had no AMA positive. Moreover, the findings showed that majority (80%) had no vaccination history. In terms of DEXA the results indicated that about 28% had DEXA, however, majority (51%) had no DEXA. Lastly, the findings indicated that serum globulin concentration <1 were found in 26% of the cases, followed by 1.5-2 (22%). However, 25% of the cases had not tested for serum globulin concentration.

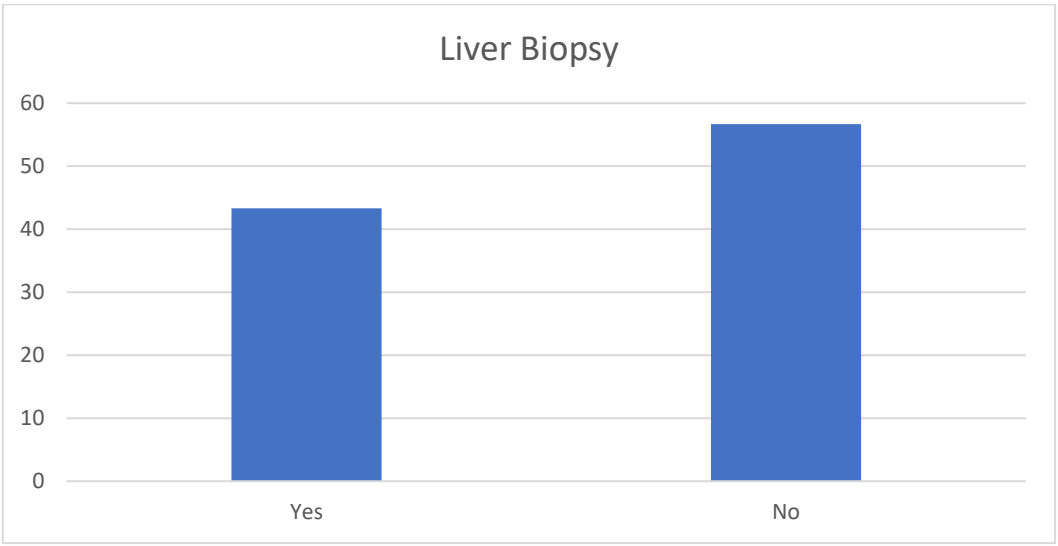

Figure 1: shows the graphical representation of Liver Biopsy

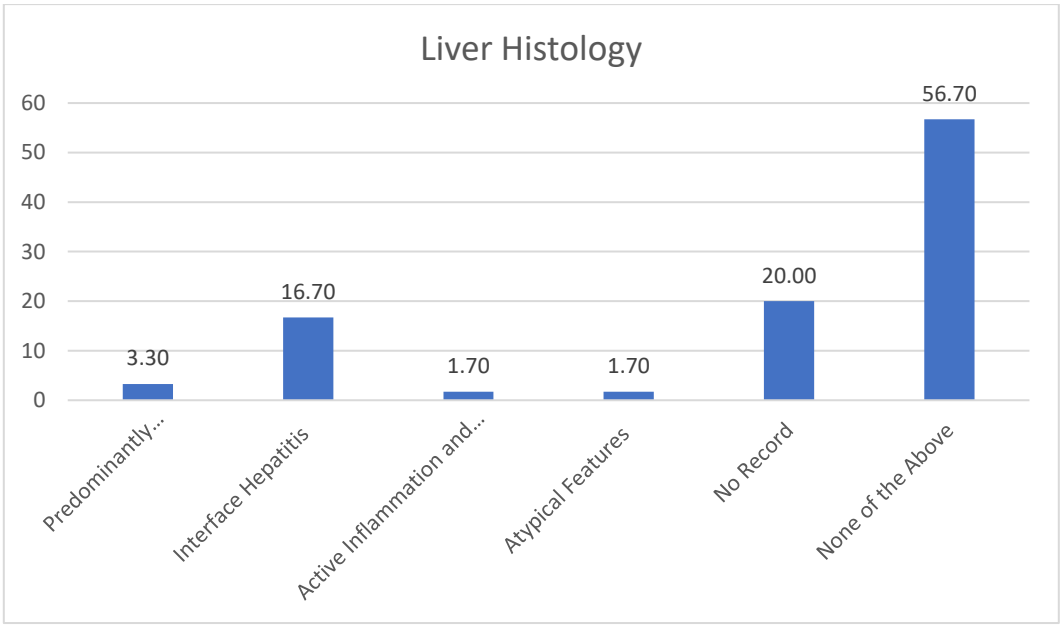

Figure 2: shows the graphical representation of Liver Histology

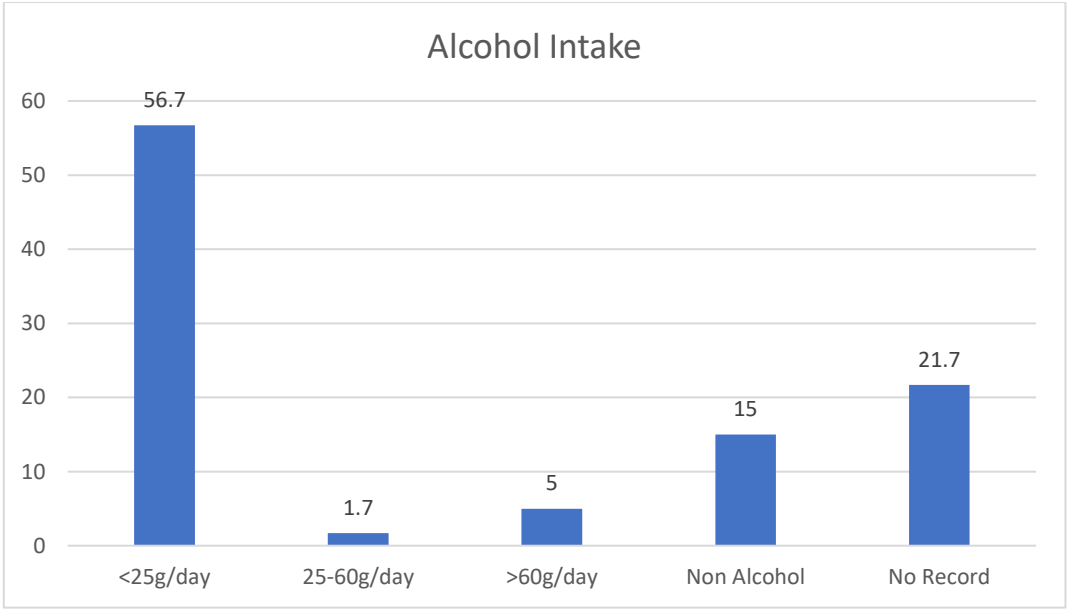

Figure 3: shows the graphical representation of Alcohol Intake

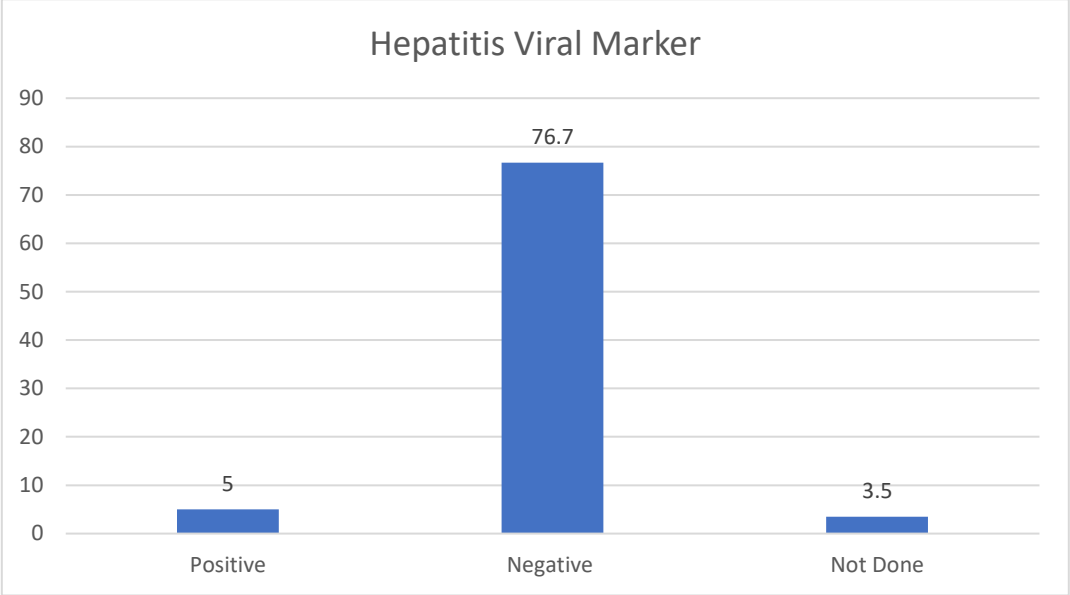

Figure 4: shows the graphical representation of Hepatitis Viral Marker

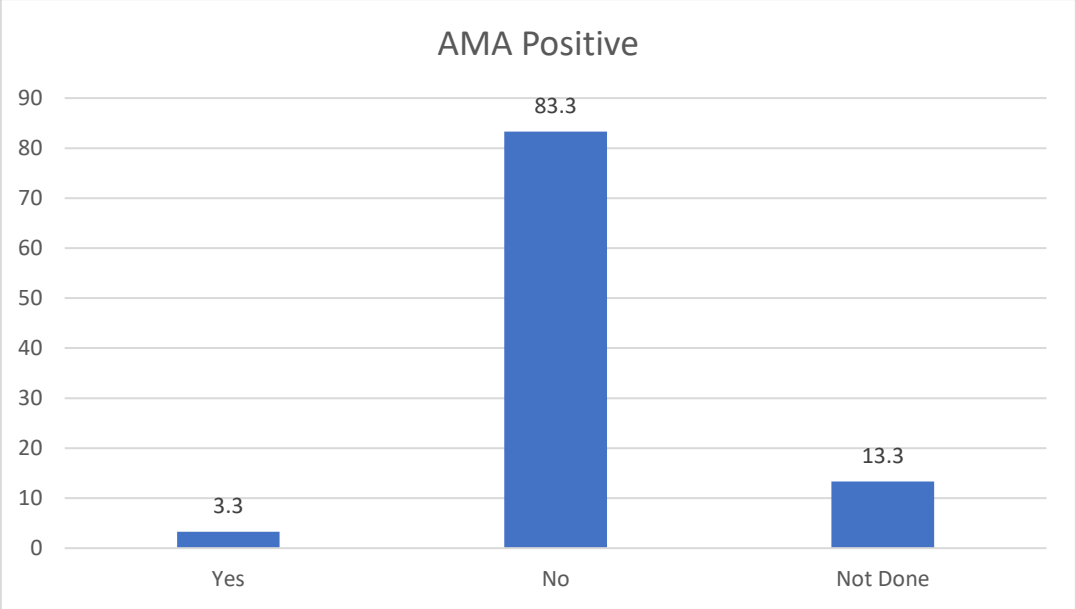

Figure 5: shows the graphical representation of AMA Positive

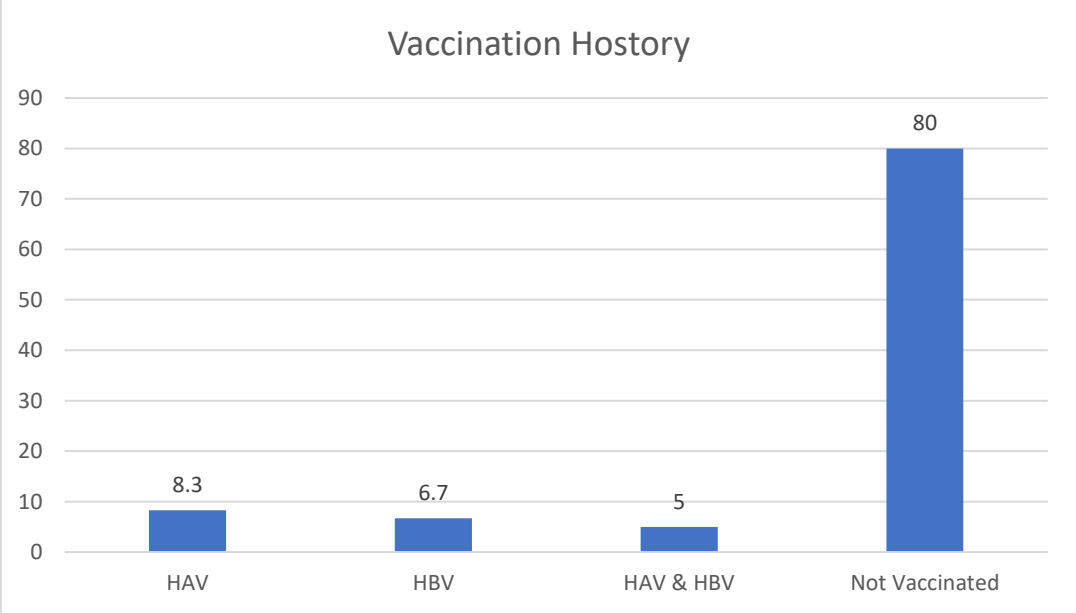

Figure 6: shows the graphical representation of Vaccination History

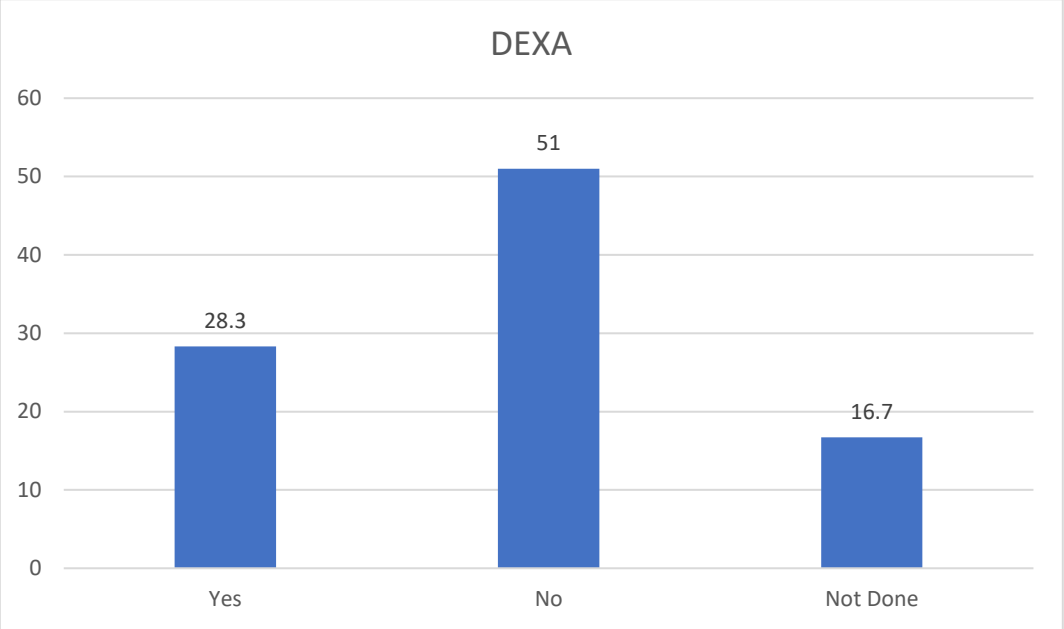

Figure 7: shows the graphical representation of DEXA

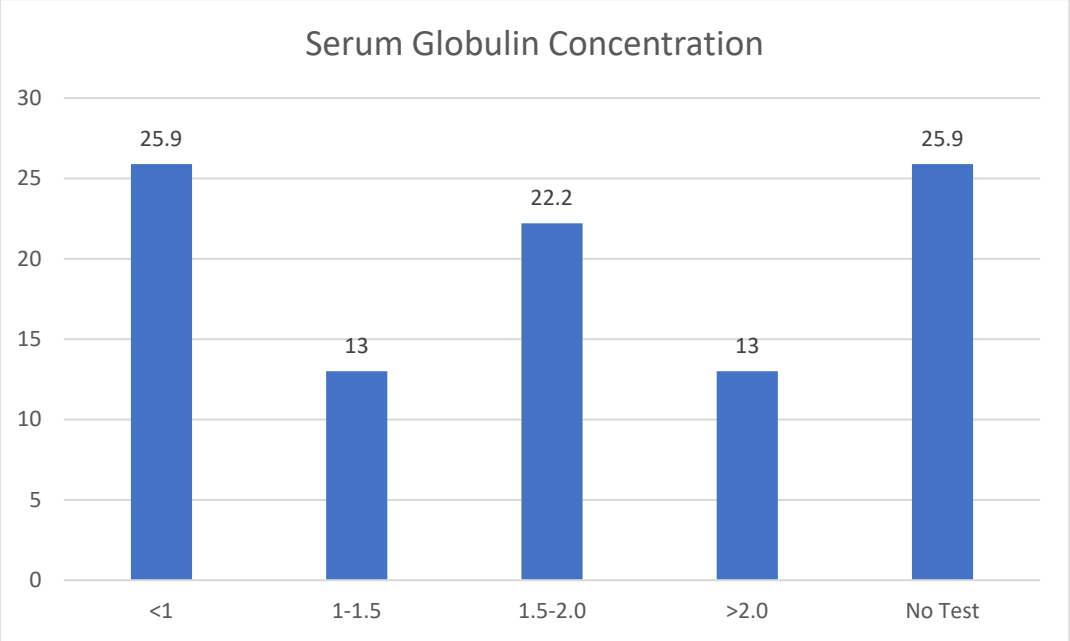

Figure 8 shows the graphical representation of Serum Globulin Concentration

Discussion

In this cohort to test the association between the lunar month of diagnosis with clinical and sociodemographic characteristics, we found that the male exhibited higher frequency on new moon than female. However, male exhibited lower frequency on full moon than female. No symptoms exhibited higher frequency on full moon than new, first quarter and third quarter moon. Moreover, the 1.5-3.0 range of ALPAST or ALT Ratio exhibited lower frequency on new moon than full, first quarter and third quarter moon. It was also observed that the Steroids and AZA treatment exhibited lower frequency on full moon and third quarter moon than new and first quarter moon. The super new moon exhibited higher frequency on new moon than new, first quarter and third quarter moon. When seeing Lunar Month of Diagnosis with Cirrhosis, patients having cirrhosis exhibited higher frequency on the first quarter and third quarter moon than new moon and full moon. Similarly, when considering Special Moon Events with Cirrhosis, having cirrhosis exhibited higher frequency on the first quarter and third quarter moon than new moon and full moon.

Pliny the Elder stated that the moon's influence "pierces all things," including plants, fish, animals, and mankind [11]. He also made the connection between the Moon and tides, which Newton validated quantitatively. The lunar surroundings in the geomagnetic tail is an exciting field of research with extensive implications for surface-bounded exospheres across our planetary system and well beyond, along with our knowledge of the classical physics of plasma discharges in delicate settings. The existence of lunar-derived plasma in the geomagnetic tail may potentially have implications for the Moon-Earth interaction. Charged particles can move from the Moon to the near-Earth environment [12], impacting the environment not just near the Moon, but also where magnetic field lines connect the Moon to the Earth's ionosphere. Plasma detected near the Moon, on the other hand, may contain material produced not just from the Moon but also from the terrestrial ionosphere [13]. A survey of recent research on the ubiquitous nature of this lunar power is confirmed by biological responses, particularly from plants and animals. However, physics computations and other reasons reject the alleged gravitational processes and light. With evidence of electromagnetic fields related with recent space travel, a new method is possible,

comparable, but more limited, effects from the Earth's magnetotail at full moon during the night, and similar, but more restricted, effects from the Earth's magnetotail at full moon during the day. At new moon during the day, the Moon's wake on the magnetosphere is visible [11].

The majority of chronobiology research has focused on solar cycles (daily and yearly); moonlight and the lunar cycle have gotten far less attention. The impacts of the moon cycle have been extensively researched in intertidal settings, with an emphasis on behaviour and reproductive synchronization [14]. The impacts of moonlight have long been recognised by terrestrial ecologists. Foraging behaviour has an impact on predation success and, as a result, predation danger and the usage of habitat [15].

The lunar cycle corresponds to the 29.5-days necessary for Moon to orbit the Earth, as well as the 24.8-hours required for the Moon to pass through the same position over the Earth [16]. These two cycles are responsible for a variety of environmental cycles, including lighting levels, tides, and geomagnetic fields. The Moon, the Earth, and the Sun are on about the same axis every 14.5 days as a result of the Moon's orbit around the Earth, and this causes spring tides. The 24.8-hour lunar day, on the other hand, results in a 12.4-hour tidal cycle, with high tides occurring when the Moon is immediately over the sea water or on the diametrically opposing point on the horizon. Finally, since the Moon's orbit deviates from the Earth's equatorial plane, the amplitude of the semidiurnal tides (with a period of 12.4 h) is asymmetrical, resulting in semidiurnal inequality in the tides, which in certain circumstances is so uneven that only one large ebb of water occurs every 24.8 h and not every 12.4 h [17]. All of these environmental changes may be recognised by animals and plants, affecting their behaviour, physiology, and the adaptive value of completing a certain activity at a specific moment, as well as their viability.

However, through research, the lunar orbit has been found to have no correlation with the induction of labor and delivery of newborns (specifically single births and first births) [18-20], menstrual cycles [21], ED and ambulance call volumes, general inpatient and critical care admission rates [22], postoperative nausea and complications [23], prison inmate outbursts and assaults [24], erratic or violent behaviors ('lunacy') [25,26], the occurrence of cardiac disease exacerbation (angina, myocardial infarction, and congestive heart failure) [27], the occurrence of trauma [28], its severity, mortality, or length of hospital stay [29], homicides [30]; and suicides [31] and even dog bites [32].

A full moon, on the other hand, has been linked to symptomatic atrial fibrillation episodes [33], paroxysmal supraventricular tachycardias [34], a slight reduction in absenteeism [35], inpatient admissions due to diarrheal illness complications [36], multiple births and births to mothers with multiple children [18], A small decrease in the number of trauma patients [37], the crime rate [38], poison centre calls and unintended ingestions [39], mental inpatient institution census [40,41], gout attacks and bronchial asthma exacerbations in children [34] have all been linked to the full moon. The new moon has been linked to a reduction in paroxysmal supraventricular tachycardias [34], as well as increases in bronchial asthma exacerbations in children [34], suicide attempts and drug usage [39], and symptomatic urine incontinence [42] retention [42], gout attacks [43].

Ethics approval and consent to participate

Not Applicable

Data Availability

All data are available in the article and further details can be requested directly from the corresponding author.

Conflicts of Interest

"The author(s) declare(s) that there is no conflict of interest regarding the publication of this paper."

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Authors' contributions

Gadour E has contributed in studies selection, data analysis, study conception and drafting of the manuscript and writing the manuscript. NP, OA and HE have contributed to the data collection, case selection, and reviewing the final manuscript. All authors have approved the final manuscript. All authors read and approved the final manuscript."

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