Neuroepidemiology study of headache in the region of Jammu of north Indian population

Amrit Sudershan
University of Jammu
Mohd Younis
Bharathair University
Aghar Chander Pushap
University Wing, Dakshina Bharat Hindi Prachar Sabha
Hardeep Kumar
Super Speciality Hospital
Srishty Sudershan
University of Jammu
Parvinder Kumar (parvinderkb2003@gmail.com)
University of Jammu

Research Article

Keywords: Headache, Prevalence, Jammu, North India, Migraine, Tension Type Headache

Posted Date: August 1st, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1894878/v1

Abstract

Background

Headache disorders represent a major public health problem globally. It is more in developing countries with the rising trends in young adults affecting negatively their quality of life. There has been very little information on the epidemiology of headache disorder in the Jammu division of the north Indian population.

Aim

The present study is aimed to find out the prevalence of headache and its two major types i.e., migraine and TTH (Tension-Type Headache) in population of Jammu division.

Methods

The study was conducted in two phases: (Phase I: Face-face interview and Phase II: E-based sampling) and sufferers of headaches were incorporated into the study based on the ICHD-3 criteria for a representative sample. Frequency distribution and mean ± SD were used in descriptive statistics to describe the data sets, while a t-test, chi-square test, and a logistic regression model using odds ratio were used in inferential statistics.

Results

A total of 3,148 subjects were recruited and found the overall prevalence of headache was 53.84% with a female preponderance (38.18%) in comparison to male 15.66%. Regarding the type, migraine was found to be highly prevalent (33.25%) type than TTH (20.58%). Female suffering from migraine shows the highest prevalence (25.28%). Regarding the environmental factors, bright light OR: 5.81, 95% CIs [4.96–6.81] loud sound OR: 5.17, 95% CIs [4.44–6.03], stress OR: 3.58, 95% CIs [3.07–4.17], empty stomach OR: 3.42, 95% CIs [2.93–3.98] increases the likely hood of the diseases. Also, high comorbidity association was found in between PCOS OR: 8.63, 95% CIs [3.95–18.85], panic disorder OR: 5.04, 95% CIs [1.94–3.05], anxiety OR: 4.53, 95% CIs [3.90–5.27], IBS OR: 3.80, 95% [1.76–8.23] with headache.

Conclusion

The prevalence of headache is high in the Jammu division of J&K India with migraine being the high prevalent type. Light and sound with high intensity, empty stomach, stress, and less water intake are some highly associated environmental risk factor that increases the severity diseases.

1. Introduction

Headache is the most common, painful, expensive, and stressful condition in the world and is mentioned as the third topmost disabling disease after low back pain and depressive disorder (**Steiner et al., 2020**). The two most prevalent neurological disorders associated with primary headaches are migraine and tension-type headaches (TTH). Global Burden Disorder- 2019 (GBD-2019) has shown that Italy shows the maximum frequency of prevalent cases per year i.e., 49.02% followed by Norway (47.98%) and Belgium (47.64%). Developed nation like USA, Russia, UK and Germany shows the prevalent rate of about 42,780.87, 40,971.76, 42,509.08 and 43,855.96 prevalent cases per 100,000 (GBD Compare | IHME Viz Hub (healthdata.org). According to the Global Burden of Disease research-2019, headache disorders were the third most frequent cause of disability out of 369 diseases and injuries (**Global Burden of Disease-2019**).

Headache has covered a significant portion of global public health issues ranging from impeding everyday functioning, loss of productivity, increasing financial burdens, and restricting social contact (Wilkes et al. 2021). Adolescents have higher rates of all types of headaches than younger children which negatively impacts their school activities, future life, and family life (Luvsannorov et al., 2020). It has been estimated that only migraine considerably causes low efficiency of job productivity with greater absenteeism and presenteeism, impairment in daily activities as well as more visits to healthcare providers. All of these significantly correlated with the cause of higher economic loss (Igarashi et al., 2020; Wong et al., 2020; Buse et al., 2020). It has been estimated that presenteeism alone costs are estimated to be over US$1296, which is higher than absenteeism costs (US$370) (Wong et al., 2020).

Although the prevalence of headache is an important epidemiologic measure and understanding the prevalence, risk factors associated with headache in populous nations like India is essential to comprehend the entire scope of the headache burden. This may have a positive impact on upcoming disease prevention and health promotion programs as well as present national or local initiatives that can benefit the healthcare system. Some studies have been conducted in different regions of India including south India and eastern India (Kulkarni et al., 2015; Ray et al., 2017) including in the Kashmir division of Jammu & Kashmir (UT) (Malik et al., 2012; Masoodi et al., 2016). But, due to the lack of headache-related studies in the division of Jammu (north Indian population), it is hard to determine how common headache issues are in the population.

Therefore, in the current study was aimed to find out the prevalence of the headache condition and its two major types including migraine and TTH in the region of the Jammu Division (**Location**: 32.73° N and 74.87° E) of the north Indian population. In addition, we evaluated the multiple environmental factors/lifestyles which may enhance the likelihood of headaches and many disorders associated with headaches, i.e., comorbidity. This is the first attempt of survey-based research in the Jammu division; hence, this insight shall provide the foundation for future research.

2. Material & Method

2.1. Sample Selection

In this survey-based epidemiological study, subjects were enrolled using a random sampling method from the Jammu division of the north Indian population, from February 2021 to April 2022. The sampling process was done in two phases, wherein phase-I, using the approach of simple random sampling, subjects were enrolled from the Jammu population by face-face interview. Each participant was briefed about the research procedure and informed consent was obtained.

But due to the COVID-19 pandemic and lockdown measures, we used E-based sampling via email with the aid of Google form (Phase II). Data collected from the E-based method was cleaned before merging with data collected from the face-to-face interview. All the incomplete data from the participants were excluded by our two authors (A.C.P & S.S).

The inclusions of migraine patients from the representative participants were based on the criteria of the International Classification of Headache Disorders - ICHD-3. Questionnaires were designed according to the ICHD-3 to diagnose the headache and its types including migraine and tension-type headaches and their features among the Jammu population. The strategy or schematic concept for selecting the sample and use of ICHD-3 criteria is depicted in the (Fig. 1).

2.2. Statistical analysis

For the descriptive data analysis of variables, mean ± standard deviation and frequency distribution were utilized for the continuous and discrete variables respectively. To find out the significant difference between the continuous variable and discrete variable, t-test and chi-square analysis were used. To establish the significant association between the environmental risk attribute and the headache, a logistic regression model using an Odds ratio (OR) with 95% confidence interval (CIs) and a p-value with < 0.05 was used. All the calculation was done using the free online statistical software including T-test calculator (graphpad.com), Chi-Square Calculator 2x2 (socscistatistics.com), and MedCalc's Odds ratio calculator. For the presentation of the association value/ OR value, “Edge weighted spring embedded layout” was used to draw the association, and Cytoscape: An Open-Source Platform for Complex Network Analysis and Visualization was utilized to draw the structure.

3. Result

3.1. Demography characteristics

A total of 3,148 subjects (24.87 ± 10.32) representing the male 1223 (38.85%) and female 1925 (61.14%) with a mean age of 25.73 ± 11.55 and 24.32 ± 9.42 respectively were included. The difference between the mean age was found to be extremely statistically significant (p value = 0.0002) and the observed difference was due to chance. The participants included were from different regions of the Jammu division, where many were seen from the Jammu district (37.26%), Kishtwar (17.24), Kathua (13.18%) Udhampur (10.10%) (Fig. 2A). Regarding the marital status of the participants, the majority were found un married (79.86%) (Fig. 2B) and concerning the occupation status of the participants, the majority were found to be students with (77.22%) **(**Fig. 2C**).** It seems that the subjects mostly favor the mixed dietary pattern including the veg and non-vegetarian, but between veg and non-vegetarian many were found to prefer the non-vegetarian diet (27.98%) (Fig. 2D). Intake of water (measured in liters) was also observed where it was found that 31.16% of participants take 2liter of water per day and more than 5 liters only 3.04%. **(**Fig. 2E**).** Other lifestyle factor estimates including smoking, alcohol, and physical activity were presented in **(**Fig. 2F**).** The detailed demographic features and frequency distribution of the participants is presented in **(**Table 1**).**

Table 1
Frequency distribution of demographic features

variable	Grouping	Total (n) (%)	Male (n) (%)	Female (n) (%)
Sample size	N/A	3148	1223	1925
Calculation	N/A	n/3148*100	n/1223*100	n/1925*100
Age	10 to 19 yrs.	1072 (34.05%)	448 (36.63%)	624 (32.41%)
	20 to 35 yrs.	1656 (52.60%)	580 (47.42%)	1076 (55.89%)
	36 to 55 yrs.	337 (10.70%)	148 (12.10%)	189 (9.81%)
	56 to 75 yrs.	84 (2.66%)	47 (3.84%)	37 (1.92%)
Marital status	Married	633 (20.10%)	274 (22.40%)	359 (18.64%)
	Unmarried	2514 (79.86%)	948 (77.51%)	1566 (81.35%)
	Divorce	1 (0.03%)	1 (0.08%)	0 (0%)
Occupation	Student	2431 (77.22%)	889 (72.69%)	1542 (80.10%)
	Govt. Job	278 (8.83%)	166 (13.57%)	112 (5.81%)
	Pvt. Job	211 (6.70%)	156 (12.75%)	55 (2.85%)
	Retired	12 (0.38%)	12 (0.98%)	0 (0%)
	House wife	216 (6.86%)	0 (0%)	216 (11.22%)
Community	Hindu	2273(72.20%)	799 (65.33%)	1474 (76.57%)
	Muslim	809 (25.69%)	405 (33.11%)	404 (20.98%)
	Sikh	61 (1.93%)	19 (1.55%)	42 (2.18%)
	Buddhist	5 (0.15%)	0 (0%)	5 (0.25%)
Water intake	< 1 l	359 (11.40%)	87 (7.11%)	272 (14.12%)
	1 l	649 (20.61%)	218 (17.82%)	431 (22.38%)
	2 l	981 (31.16%)	397 (32.46%)	584 (30.33%)
	3 l	623 (19.79%)	260 (21.25%)	363 (18.85%)
	4 l	273 (8.67%)	129 (10.54%)	144 (7.48%)
	5 l	167 (5.30%)	83 (7.78%)	84 (4.36%)
	> 5 l	96 (3.04%)	49 (4.006%)	47 (2.44%)
Diet	Veg	1608 (51.08%)	486 (33.73%)	1122 (58.28%)
	Non-veg	881 (27.98%)	406 (33.19%)	475 (24.67%)

variable	Grouping	Total (n) (%)	Male (n) (%)	Female (n) (%)
	Both	659 (20.93%)	331 (27.06%)	328 (17.03%)
Caffeine	N/A	2237 (71.06%)	855 (69.91%)	1382 (71.79%)
Dairy Product	N/A	2547 (80.90%)	951 (77.75%)	1596 (82.90%)
Junk Food	N/A	1546 (49.11%)	542 (44.31%)	1004 (52.15%)
Smoking	N/A	135 (4.28%)	115 (9.40%)	20 (1.03%)
Alcohol	N/A	157 (4.98%)	135 (11.03%)	22 (1.14%)

3.2. Prevalence

In the present epidemiology study, the prevalence rate of headache was found near 53.84% with a mean age of 24.95 ± 10.06. Representing the total prevalence of males with a mean age of 25.83 ± 11.51, it was nearly 15.66% in compression to females (24.59 ± 9.39) where the rate was high quite 38.18%.

After sub-grouping of the “headache diagnosed participants” based on the criteria “where did they belong to?”, the maximum prevalence was observed in the district of Jammu (41.23%) followed by the Kishtwar (16.99%), Kathua (11.44%), and Udhampur district (10.10%). The frequency distribution of headache prevalence is presented in the Jammu & Kashmir map (Fig. 3).

We also analyzed the different types of headaches, majorly the migraine “a neurovascular inflammatory disorder”, menstrual migraines/ hormonal headaches, and Tension-type Headache (TTH) (a stress-related headache). We observed that the prevalence of migraine was found 33.25% with males (24.45 ± 10.76) representing the total prevalence of 7.97% and females (24.23 ± 9) near 25.28%. Also, the “mensuration migraine” prevalence of 11.34%. Another headache type that we observed was TTH, where the total prevalence was found near 20.58% with males representing 12.89% and female was 7.68%.

Grouping headache subjects on the bases of the “age group”, it was observed that the highest prevalence was found in the age group of 20–35 years (mean age: 23.79 ± 4.03) (young adults) representing 55.28% with female dominance i.e., 75.77% (male:24.22%) (Table 2). Migraine was found to be more prevalent (58.07%) in the same age group (20–35 years) than TTH (50.77%). But in the middle-aged group (36–55 years), the prevalence of TTH was slightly increased (13.27%) than migraine (9.83%).

Table 2
Grouping of headache subjects using different age groups

Age Group	Mean ± SD		Headache (n = 1695) (n) (%)	Migraine (n = 1047) (n) (%)	TTH (n = 648) (n) (%)
10–19 (Adolescent)	17.65 ± 10.33	Total	532 (31.38%)	315 (30.08%)	217 (33.48%)
		Male	184 (34.58%)	88 (27.93%)	96 (44.23%)
		Female	348 (65.41%)	227 (72.06%)	121 (55.76%)
20–35 (YA)	23.79 ± 10.33	Total	937 (55.28%)	608 (58.07%)	329 (50.77%)
		Male	227 (24.22%)	127 (20.88%)	100 (30.39%)
		Female	710 (75.77%)	481 (79.11%)	229 (69.60%)
36–55 (MAG)	44.16 ± 10.35	Total	189 (11.15%)	103 (9.83%)	86 (13.27%)
		Male	65 (34.39%)	26 (25.24%)	39 (45.34%)
		Female	124 (65.60%)	77 (74.75%)	47 (54.65%)
56–75 (OAA)	61.21 ± 10.39	Total	37 (2.18%)	21 (2.00%)	16 (2.46%)
		Male	17 (45.94%)	10 (47.61%)	7 (43.75%)
		Female	20 (54.05%)	11 (52.38%)	9 (56.25%)

YA: Young Adults, **MAG**: Middle Aged Group, **OAA**: Old Age Group

3.3. Association of environmental risk factors

As the study was not restricted to finding the condition prevalence, we also explored the different environmental risk attributes/lifestyle risk attribute which may contribute to the disease's likelihood. A diverse range of factors was found to be associated with headache which significantly increases the chance of diseases (Fig. 4).

Stress, an inevitable factor contributes significantly to the likelihood of the diseases with an associated value of OR: 3.58, 95% CIs [3.07–4.17] ($p < 0.0001$). After analyzing the different forms of stress, educational stress {OR: 3.41 [2.81–4.12] ($p < 0.0001$)} was found to be more effective than emotional OR: 3.02, 95% CIs [2.38–3.83] ($p < 0.0001$), and physical stress which include the extreme household work, long working hours, etc. OR: 2.07, 95% CIs [1.42–3.02] ($p = 0.0001$). Proper sleep is considered a good indicator of a healthy life but a loss of sleep is a major contributor to the risk of various diseases. In this respect, we also found that sleep less significantly impacted the risk of headache (OR: 2.19, 95% CIs [1.83–2.62] ($p < 0.0001$). Stress causes significant loss of sleep with an association value OR: 2.28, 95% CIs [1.8784–2.7854] ($p < 0.0001$).

We have also observed that headache subjects were significantly associated with the low water intake, including < 1 liter with an association ration of OR: 2.50, 95% CIs [1.97–3.17] (p-value: <0.0001), 2 liter OR:

1.34, 95% CIs [1.13–1.59] ($p = 0.007$), and 3 liter OR: 1.1, 95% CIs [0.94–1.49] ($p = 0.14$). Regarding the dietary habit, red meat/ non-vegetarian food was not found to be associated with the risk of headache OR: 1.00, 95% CIs [0.85–1.18] ($p = 0.9487$), but on the other hand junk food, dairy products (such as milk, curd, ice-creams, etc.) and caffeine intake were found to be significantly associated with the condition with an OR: 1.95, 95% CIs [1.69–2.25] ($p < 0.0001$), OR: 1.36, 95% CIs [1.14–1.62] ($p = 0.0006$) and OR: 0.80, 95% CIs [0.70–0.91] ($p = 0.0015$) respectively. Also, it was observed that an empty stomach increases the risk of the condition by 3.4% (OR: 3.42, 95% CIs [2.93–3.98] ($p < 0.0001$).

Changes in the weather condition have also been found to increase the risk of headaches whereas the hot temperature was found to increase the risk by 2.3% (OR: 2.35, 95% CIs [1.88–2.95] ($p < 0.0001$). Bright light including bright sunlight, high beam light, flashing/ flickering of light, and sound (loud sound) was found a major risk factor for headache, increasing the risk by OR: 5.81, 95% CIs [4.96–6.81] ($p < 0.0001$) and OR: 5.17, 95% CIs [4.44–6.03] ($p < 0.0001$).

To this end, a lot of environmental risk factors have been found which are presented in the frequency weighted association graph (Fig. 3) to be significantly associated with the risk of headache. As we know, minimizing the interaction with the environmental risk factor can significantly minimize the risk of headache.

3.4. Comorbidity

In the present study we have also explored the comorbidities associated with headache. As a result, different diseases were found such as Hypo Thy (Hypothyroidism). OR: 2.5886, 95% CIs [1.0248–6.5386] ($p = 0.0442$), IBS (Irritable Bowel Syndrome) OR: 3.8084, 95% [1.7610–8.2360] ($p = 0.0007$), PCOS (Poly cystic Ovarian Syndrome) OR: 8.6336, 95% CIs [3.9528–18.8570] ($p < 0.0001$), anxiety OR: 4.5373, 95% CIs [3.9000-5.2787] ($p < 0.0001$), hypertension (HT) OR: 2.9246, 95% CIs [1.9785–4.3231] ($p < 0.0001$), depression OR: 1.9363, 95% CIs [1.1651–3.2181] ($p = 0.0108$), panic disorder (PD) OR: 5.0411, 95% CIs [1.9463–3.0570] ($p = 0.0009$), uric acid (UA) OR: 4.7390, 95% CIs [1.0487–2.14158] ($p = 0.0432$). All the comorbidity association presented in the ORs weighted comorbidity graph (Fig. 5). Significant differences have been found with respect to their frequency in between headache and non-headache.

4. Discussion

4.1. Prevalence rate

The Global Burden of Disease (GBD)-2019 has revealed that headache prevalence is much higher in the top economically developed nations, with the greatest prevalence rates being observed in Italy (49.02%) and the USA (45.11%). Regarding the India's neighbouring countries and the states of India, the highest prevalence has been recorded in Sri Lanka (37.2%) followed by Nepal (35.95) and the states of Sikkim (38.08%) and Goa (35.24%) respectively (**Global Burden of Disease (GBD)-2019**).

In the current study, high headache prevalence estimates were found (Fig. 3) which is also consistent with the other epidemiological study conducted in different regions of India. In south India, headache prevalence is 63.9% with a female preponderance of 73% in comparison to male (54.4%), TTH is 34.8% and migraine 25.6% (female:32.4% & male: 18.6%) (Kulkarni et al., 2015). In the eastern states of India, headache prevalence was 14.87% where the females were 23.51% and males were 5.44 and migraine was 14.12% (males: 5.35% and 22.16%) (Ray et al., 2017). In the north Indian region, different studies have shown that the headache prevalence is 63.9% wherein females were found to be more affected (74.3%) as compared to males (32.6%). Prevalence of migraine was 13.44% with a female preponderance (87.5%) **(Nandha et al., 2013).** A prospective observational study in the north Indian population found that 67.7% of patients had migraine and 32.2% of patients had tension-type headaches (TTH) (Sastry et al., 2022). In the valley of Kashmir, headache in the pediatric population was observed where the frequency was found at 66.4% with the female at 65.15% and male at 35.85%, Migraine at 26.98%, and TTH at 50.99% (Malik et al., 2012). Another group found the headache frequency rate equal to 66.20% (19–45 years) with female dominancy (61.82%) to male (38.18%). In migraine, the total prevalence was found 45.69% with 55.44% in females and 32.0% in males (Masoodi et al., 2016).

To this end, the prevalence of headache and its type varies from region to region and this disparity is mighty due to the different sampling approach (simple random, clustered, stratified sampling), different sample size, type of study (population-based/ hospital case-control, cohort), the differing methodology adopted, differences in defining the criteria of headache prevalence (1 year vs. 3 months), coexisting environmental factors, urban/rural differences, or ethnicity of the studied population.

4.2. Environmental risk factors

Headaches were strongly connected with concurrent disorders, routine drug use, analgesic use for diseases other than headaches, and a variety of environmental risk variables (Nieswand et al. 2019). In the present study, different environmental factors have been observed which increase the risk of condition significantly (Fig. 4).

In the present study, bright light was found significantly ($p < 0.0001$) associated with headache (OR: 5.81) and various studies have supported the fact that bright light within the range of 450 nm to 578 nm wavelength significantly alter the condition (Drummond, 1986; Main et al., 2000; Ofovwe & Ofili, 2010). Bright light significantly excites the nociceptive neurons in superficial laminae of trigeminal subnucleus caudalis (Vc/C1) mediated by an intraocular mechanism and transmission through the TRG (Trigeminal root ganglion) (Okamoto et al., 2010) and responsible for pain (Moulton et al., 2009). Bright light also modulates the dura-sensitive neurons in the posterior thalamus whose axons are projected extensively across layers I–V of somatosensory, visual, and associative cortices. The cell bodies and dendrites of such dura/light-sensitive neurons were opposed by axons originating from retinal ganglion cells (RGCs), predominantly from intrinsicality photosensitive RGCs (Retinal Ganglion Cells) (Noseda et al., 2010). Other than the classical pathways, a research study has also supported the other non-classical pathway mediated through the melanopsin, a photopigment that underlies subconscious vision, in the trigeminal nerve (Matynia et al., 2016). CGRP (Calcitonin Gene Related Peptide), a potent vasodilator has been found to mediate the transfer of bright light stimulus and anti-CGRP or vasoconstrictive agents blocked light-evoked neural activity (Okamoto et al., 2010; Navratilova et al., 2019).

Weather is another interesting risk factor that have been found to be a profound risk attribute of headaches, as we have also observed that different weather conditions significantly increase the likelihood of headaches (**See Result section**). In support of our study, other studies have shown that weather changes act as a trigger for headache onset or the worsening of ongoing headache symptoms (Prince et al., 2004). Lower temperature and higher relative humidity have been significantly associated with the onset of a migraine period (Hoffmann et al., 2011). Increases and decreases in temperature lead to a significant increase in the number of migraine attacks (Scheidt et al., 2013). Temperature change accounted for 16.5% of the variance in headache incidence in winter and 9.6% in summer (Yang et al., 2015). This high variance is due to the variance for the temperature and sunshine duration, followed by humidity and pressure during cold (Yang et al., 2011).

TRPM8 (Transient receptor-potential M8), a cation channel (Na^+ and Ca^{++}) is the prime candidate for temperature sensation and is expressed in pain sensory neurons (McKemy et al., 2002) Genome-wide association studies (GWAS) have implicated the TRPM8 channel in association migraine (Hautakangas et al., 2022) and it has been found that decreased expression of *TRPM8* is associated with a reduced risk for migraine where homozygous carriers of rs10166942[C] were less sensitive to cold pain (McKemy et al., 2002).

Stress can be physiological and oxidative wherein physiological stress includes social support, loneliness, marriage status, social disruption, work environment, social status, social integration, etc, and oxidative represents the increased reactive oxygen species and reactive nitrogen species in the blood. Other than oxidative, physiological stress has greatly influenced the headache where it is found that an increase in the stress intensity will increase the headache frequency (Schramm et al., 2015). Different forms include occupational stress (Lin et al., 2007; **Gillespie et al., 2015;** Godwin et al., 2016), educational stress (Ghorbani et al., 2013; Ibrahim et al., 2017) have been found to be associated with headaches.

Sleep quality is closely linked to headache (**Yokoyama et al., 2019**), which affects around 30–50% of migraine patients, and is one of the reasons why migraine sufferers are prone to morning headaches because of sleep deprivation. The impact of sleep disturbances increases self-reported pain and leads to a disturbance of the descending pain inhibitory control system (Lin et al., 2016; Negro et al 2020).

Another important risk factor that was found to be significantly associated with the condition was less water intake (**See Result Section**). In support of our study, various studies have found that water deprivation may play a role in migraine, particularly in prolonging attacks (Blau et al., 2004), and drinking more water resulted in a statistically significant improvement (Price & Burls, 2015). This water ingestion provided relief from headache within 30min to 3hr. It is proposed that water deprivation-induced headache is the result of intracranial dehydration and total plasma volume (Popkin et al., 2010). Studies have also shown that water intake did not affect the number of headache episodes, but was associated modestly with a reduction in headache intensity and reduced duration of headache (Spigt et al., 2005). Despite such benefits of water intake, it has also been shown that headache is also caused by drinking cold water which is called “ice-water stimulus provoked headache” attributed to ingestion or inhalation of a cold stimulus (Mages et al., 2017) and this pain perception is induced by a cold palatal stimulus (Mattsson, 2001; Mages et al., 2017). There has been also reported that there has a negative correlation between water intake and the frequency of headaches. (Khorsha et al., 2020).

The most extensively used psychostimulant substance in the world is caffeine, also known as trimethylxanthine, an alkaloid that occurs naturally in several plants. The current study provides insight into the risk-attribution potential of caffeine by demonstrating its modest risk capability which significantly ($p < 0.0001$) increases the chance of condition by 1.95fold. In support of our study, population-based cases and controls have found that patients with chronic daily headache (CDH) were more likely overall to have been high caffeine consumers before the onset of CDH (Scher et al., 2004). Also, a prospective cohort study, conducted by Mostofsky and the group found that high levels of caffeinated beverage intake may be a trigger of migraine headaches (Mostofsky et al., 2019). It has also been shown that the sudden cessation of caffeine use after chronic exposures leads to a withdrawal syndrome with headache as a dominant symptom (Shapiro, 2008), constipation, impaired behavioural and cognitive performance, joint pains, decreased or increased blood pressure, increased heart rate, hand tremor, increased diuresis, and abdominal pain (Juliano & Griffiths, 2004; **Meredith et al., 2013).**

But in contrast to its risk attribution, with intermittent exposure, caffeine may act as a mild analgesic for headache or as an adjuvant for the actions of other analgesics (Shapiro, 2008). The doses of 130 mg enhance the efficacy of analgesics in TTH and doses of ≥ 100 mg enhance benefits in migraine (Lipton et al., 2017). It is not recommended to exceed 400–450 mg/day, because chronic repetitive exposures to caffeine increase the risks for the development of analgesic-overuse headache, and chronic daily headache (Hering-Hanit & Gadoth, 2003). Caffeine is rapidly and completely absorbed into the bloodstream after oral ingestion, with peak blood levels reached in 30 min to 45 min. Caffeine with a typical half-life of four to six hours is metabolized by the liver and is excreted by the kidneys via urine **(Meredith et al.2013)**. Caffeine molecules are structurally similar to adenosine and bind to adenosine receptors on the cell surface and act as competitive inhibitors. As the inhibitory effect of caffeine on adenosine receptors, the state of cortical hyperexcitability is established and this increases alertness and improves cognitive function (Espinosa Jovel & Sobrino Mejía, 2017). Also, caffeine releases dopamine and stimulates glucose utilization in the prefrontal cortex and a caudate nucleus respectively which help in positive reinforcement and mediates motor activity and regulate the sleep-wake cycle respectively (O'Callaghan et al., 2018).

We also observed that empty stomach/ fasting significantly ($p < 0.0001$) increases the likelihood of headache by 3.42fold, which is also supported by various epidemiological studies (Bánk & Márton, 2000; Abu-Salameh et al., 2010). The length of the fasting-induced headache is dependent on the length of the fast and pain is featured as non-pulsating, mild to moderately intense, wide, or centred in the frontal area (Torelli & Manzoni, 2010). The fact has also been supported that after a long time if an individual takes a meal, the chance of postprandial fasting-related headaches increases which is featured with episodic in nature, heaviness (AlAmri et al., 2021). The proposed mechanism depicts that a network of neurons and astrocytes may collectively depolarize as a result of an imbalance between the excitatory and inhibitory processes set by a lack of glycogen-derived glucose at the start of intensive synaptic activity. Activating pannexin1 channels in neurons and starting parenchymal inflammatory pathways, may stimulate perivascular trigeminal afferents **(Dalkara & Kilic, 2013).**

In addition, dietary habit such as consumption of red meat/ non-vegetarian food was not found significantly (($p = 0.9487$) associated with headache but on the other hand junk food, dairy products (such as milk, curd, ice-creams, etc.) significantly associated with the condition with an OR: 1.95, 95% CIs [1.69–2.25] ($p < 0.0001$), OR: 1.36, 95% CIs [1.14–1.62] ($p = 0.0006$). Regarding diary products conflicting result have been reported (Mansouri et al., 2020) and patients with migraines consumed less milk than people without migraines (Nazari & Eghbali, 2012; Rist et al., 2015).

Enclosing the section, the present epidemiology study has presented a various range of environmental risk attributes that significantly increases the likelihood of headache. Patients with headaches need to be enlightened about the risk factors that contribute to their condition so that they can avoid them and possibly reduce their headache frequency.

4.3. Comorbidities

Co-morbidity is another great thing of concern that needs to be thought about and is defined as the presence of two or more chronic conditions at the same time (Valderas et al., 2009). Comorbidity with headache is a common concern, with more than a third of patients seen by primary care physicians having four or more chronic health issues, and a small percentage having more than ten.

In the present epidemiological study, various condition has been found to be associated with headache (Fig. 5). As in the present study, IBS was found to be highly associated with headache {OR: 3.8084, 95% [1.7610–8.2360] ($p = 0.0007$)}. Different epidemiological research from different parts of the world has shown the high rates of co-existing IBS and headache which supports our research (Chang & Lu, 2013; Lau et al., 2014; **Mirzaei et al.,2016;** Li et al., 2017; Kawashima et al., 2020; Grover et al., 2021). Headache sufferers specifically migraineurs with long headache history and high headache frequency have a higher chance of being diagnosed with IBS. IBS and migraine share some similarities and can alter gut microflora composition and thereby may affect the gut-brain axis and inflammatory status (Arzani et al., 2020). A key neurotransmitter i.e., serotonin plays a role in both conditions, wherein IBS serotonin causes excessive bowel motions, a lot of digestive output, as well as visceral hypersensitivity in the gut, and defective serotonin activity in the central nervous system is responsible for the migraine. (Camilleri, 2009). In addition, individuals with IBS and migraine have been found to have high family aggregation and genetic variations, such as those in the serotonin reuptake transporter gene (5-HTTLPR) (Schürks et al., 2010; Zhang et al., 2014).

Other than IBS, PCOS was also found to be significantly ($p < 0.0001$) associated with headache (OR: 8.6336). Different studies have shown that women with PCOS are burdened with multimorbidity which includes hypertension, tendinitis, osteoarthritis, fractures, endometriosis, and importantly migraine (Glintborg et al., 2015; **Banday et al., 2022** Kujanpää et al., 2022). The PCOS-disease subnetworks were subjected to pathway enrichment analysis and found a substantial relationship between PCOS and other illnesses like hypertension and migraine (Ramly et al., 2019). Other conditions like anxiety, hypertension, depression, and panic disorder are also comorbid conditions associated with the headache (Muayqil et al., 2018; Caponnetto et al., 2021; Togha et al., 2022) including uric acid and (Yazar et al., 2021) and hypothyroidism (**Lima et al., 2017;** Rubino et al., 2019; Spanou et al., 2019). Increased levels of uric acid and serum cholesterol have been reported to strongly correlate with white matter hyperintensities; this association may be explained by altered endothelial dysfunction and increased attack frequency (Trauninger et al., 2011).

Comorbidity of diseases with headaches may be due to several reasons some of which include sharing common pathophysiological mechanisms (**Lauritzen et al., 2011)**, common risk factors including the common genetic variants, and common environmental risk factors. Comorbidity with common diseases is mostly concerned with the sharing of common risk attributes which are frequently used whether it is genetic or environmental factors.

5. Conclusion

Headache affects millions of individuals across the country and is defined as a complicated neurovascular condition, not merely a simple discomfort. Many different diseases are linked with headaches and a diverse range of environmental, lifestyle and genetics factors have been observed. Therefore, limiting the exposure to environmental factors could decrease the likelihood of occurrence of headache. Hence, the headache is found to be a highly prevalent neurovascular condition among the people of Jammu division of the north Indian population.

List Of Abbreviations

TTH
Tension-type headache
GBD
Global burden Disorder
UT
Union Terr
ICHD-3
International Classification of Headache Disorder-3
OR
Odds Ratio
CIs

Confidence Interval

IBS

Irritable Bowel Syndrome

PCOS

Polycystic Ovarian Syndrome

USA

United States of America

TRG

Trigeminal root ganglion

RGCs

Retinal Ganglion Cells

CGRP

Calcitonin Gene-Related Peptide

TRPM8

Transient receptor-potential M8

GWAS

Genome-Wide Association study

Declarations

Statement of Ethics: The present study design was duly approved by the Institutional Ethical Committee (IEC), University of Jammu vide notification number EC: DRS/22/4969) and Institutional Ethics Committee, Government Medical College, Jammu (ECR/454/Inst/JK/2013/RR-20). **Consent to participate:** Data was done after having informed written consent from each study participant.

Consent for publication: Not applicable

Data Availability Statement: The data from the current study is unavailable to the public due to restrictions. Interested researchers should contact **Dr. Parvinder Kumar** (Parvinderkb2003@gmail.com) who oversaw the data collection.

Conflict of Interest Statement: The authors declare that they have no conflict of interest.

Funding Sources: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author Contributions: Dr. Parvinder Kumar & Amrit Sudershan contribute to the study design, **Amrit Sudershan, Dr. Mohd. Younis, Agar Chander Pushap & Srishty Sudershan** Conducted the survey, **Agar Chander Pushap & Srishty Sudershan** helped with data cleaning, **Agar Chander Pushap & Amrit Sudershan** analysed the data. **Amrit Sudershan & Dr. Mohd Younis** drafted the manuscript and edited the pictures and table. **Dr. Parvinder Kumar & Dr. Mohd. Younis** edited the manuscript**, Dr. Parvinder Kumar** finalize the manuscript.

Acknowledgment: Authors are thankful to the Institute of Human Genetics, University of Jammu, **Dr. Pragya Khanna** (Principal at GLDM Degree College Hiranagar, Jammu, Jammu & Kashmir-UT), **Dr. Roopali Fotra** (Department of Zoology), **Dr. Sanjay Bhagat** (Indira Gandhi Govt. *Dental College, Jammu, Jammu & Kashmir-UT), **Shikha Sharma** (Research scholar at Department of Zoology, Lovely Professional University, Phagwara, Punjab) for their valuable support during the sampling period.*

References

1. Steiner, T. J., Stovner, L. J., Jensen, R., Uluduz, D., Katsarava, Z., & Lifting The Burden: the Global Campaign against Headache (2020). Migraine remains second among the world's causes of disability, and first among young women: findings from GBD2019. The journal of headache and pain, *21*(1), 137. https://doi.org/10.1186/s10194-020-01208-0
2. GBD 2019 Diseases and Injuries Collaborators (2020). Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet (London, England), *396*(10258), 1204–1222. https://doi.org/10.1016/S0140-6736(20)30925-9
3. Wilkes, M.J., Mendis, M.D., Bisset, L., Leung, F. T., Sexton, C. T., & Hides, J. A. (2021). The prevalence and burden of recurrent headache in Australian adolescents: findings from the longitudinal study of Australian children. The Journal of Headache and Pain, 22(49), 1–13. https://doi.org/10.1186/s10194-021-01262-2
4. Luvsannorov, O., Anisbayar, T., Davaasuren, M., Baatar, O., Batmagnai, K., Tumurbaatar, K., Enkhbaatar, S., Uluduz, D., Sasmaz, T., Solmaz, E. T., & Steiner, T. J. (2020). The prevalence of headache disorders in children and adolescents in Mongolia: a nationwide schools-based study. The Journal of Headache and Pain, 21(107), 1–9 https://doi.org/10.1186/s10194-020-01175-6.
5. Igarashi, H., Ueda, K., Jung, S., Cai, Z., Chen, Y., & Nakamura, T. (2020). Social burden of people with the migraine diagnosis in Japan: evidence from a population-based cross-sectional survey. BMJ open, 10(11), e038987. https://doi.org/10.1136/bmjopen-2020-038987
6. Wong, L. P., Alias, H., Bhoo-Pathy, N., Chung, I., Chong, Y. C., Kalra, S., & Shah, Z. (2020). Impact of migraine on workplace productivity and monetary loss: a study of employees in banking sector in Malaysia. The journal of headache and pain, 21(1), 68. https://doi.org/10.1186/s10194-020-01144-z
7. Buse, D. C., Yugrakh, M. S., Lee, L. K., Bell, J., Cohen, J. M., & Lipton, R. B. (2020). Burden of Illness Among People with Migraine and ≥ 4 Monthly Headache Days While Using Acute and/or Preventive Prescription Medications for Migraine. Journal of managed care & specialty pharmacy, 26(10), 1334–1343. https://doi.org/10.18553/jmcp.2020.20100
8. Kulkarni, G. B., Rao, G. N., Gururaj, G., Stovner, L. J., & Steiner, T. J. (2015). Headache disorders and public ill-health in India: prevalence estimates in Karnataka State. The journal of headache and pain, 16, 67. https://doi.org/10.1186/s10194-015-0549-x
9. Ray, B. K., Paul, N., Hazra, A., Das, S., Ghosal, M. K., Misra, A. K., Banerjee, T. K., Chaudhuri, A., & Das, S. K. (2017). Prevalence, burden, and risk factors of migraine: A community-based study from

Eastern India. Neurology India, 65(6), 1280–1288. https://doi.org/10.4103/0028-3886.217979

10. Malik, A. H., Shah, P. A., & Yaseen, Y. (2012). Prevalence of primary headache disorders in school-going children in Kashmir Valley (North-west India). Annals of Indian Academy of Neurology, 15(Suppl 1), S100–S103. https://doi.org/10.4103/0972-2327.100030
11. Masoodi, Z. A., Shah, P. A., & Iqbal, I. (2016). Prevalence of headache in Kashmir Valley, India. Neurology Asia, 21(2).
12. Nandha, R., & Chhabra, M. K. (2013). Prevalence and clinical characteristics of headache in dental students of a tertiary care teaching dental hospital in Northern India. Int J Basic Clin Pharmacol, 2(1), 51–55.
13. Sastry, A. S., Kumar, A., Pathak, A., Chaurasia, R. N., Singh, V. K., Joshi, D., Singh, V., & Mishra, V. N. (2022). The pattern of primary headache in the North India population: a hospital-based study. The International journal of neuroscience, 1–9. Advance online publication. https://doi.org/10.1080/00207454.2022.2075359
14. Nieswand, V., Richter, M., Berner, R., von der Hagen, M., Klimova, A., Roeder, I., Koch, T., Sabatowski, R., & Gossrau, G. (2019). The prevalence of headache in German pupils of different ages and school types. Cephalalgia, 39(8), 1030–1040. https://doi.org/10.1177/0333102419837156
15. Drummond, P. D. (1986). A quantitative assessment of photophobia in migraine and tension headache. Headache: The Journal of Head and Face Pain, 26(9), 465–469.
16. Main, A., Vlachonikolis, I., & Dowson, A. (2000). The wavelength of light causing photophobia in migraine and tension-type headache between attacks. Headache: The Journal of Head and Face Pain, 40(3), 194–199.
17. Ofovwe, G. E., & Ofili, A. N. (2010). Prevalence and impact of headache and migraine among secondary school students in Nigeria. Headache: The Journal of Head and Face Pain, 50(10), 1570–1575.
18. Okamoto, K., Tashiro, A., Chang, Z., & Bereiter, D. A. (2010). Bright light activates a trigeminal nociceptive pathway. PAIN®, 149(2), 235–242.
19. Moulton, E. A., Becerra, L., & Borsook, D. (2009). An fMRI case report of photophobia: activation of the trigeminal nociceptive pathway. Pain, 145(3), 358–363.
20. Noseda, R., Kainz, V., Jakubowski, M., Gooley, J. J., Saper, C. B., Digre, K., & Burstein, R. (2010). A neural mechanism for exacerbation of headache by light. Nature neuroscience, 13(2), 239–245. https://doi.org/10.1038/nn.2475
21. Matynia, A., Nguyen, E., Sun, X., Blixt, F. W., Parikh, S., Kessler, J., … Gorin, M. B. (2016). Peripheral sensory neurons expressing melanopsin respond to light. Frontiers in Neural Circuits, 10, 60.
22. Navratilova, E., Rau, J., Oyarzo, J., Tien, J., Mackenzie, K., Stratton, J., … Porreca, F. (2019). CGRP-dependent and independent mechanisms of acute and persistent post-traumatic headache following mild traumatic brain injury in mice. Cephalalgia, 39(14), 1762–1775.
23. Prince, P. B., Rapoport, A. M., Sheftell, F. D., Tepper, S. J., & Bigal, M. E. (2004). The effect of weather on headache. Headache: The Journal of Head and Face Pain, 44(6), 596–602.

24. Hoffmann, J., Lo, H., Neeb, L., Martus, P., & Reuter, U. (2011). Weather sensitivity in migraineurs. Journal of neurology, 258(4), 596–602.
25. Scheidt, J., Koppe, C., Rill, S., Reinel, D., Wogenstein, F., & Drescher, J. (2013). Influence of temperature changes on migraine occurrence in Germany. International journal of biometeorology, 57(4), 649–654.
26. Yang, A. C., Fuh, J. L., Huang, N. E., Shia, B. C., & Wang, S. J. (2015). Patients with migraine are right about their perception of temperature as a trigger: time series analysis of headache diary data. The journal of headache and pain, 16(1), 1–7.
27. Yang, A. C., Fuh, J. L., Huang, N. E., Shia, B. C., Peng, C. K., & Wang, S. J. (2011). Temporal associations between weather and headache: analysis by empirical mode decomposition. PloS one, 6(1), e14612.
28. McKemy, D. D., Neuhausser, W. M., & Julius, D. (2002). Identification of a cold receptor reveals a general role for TRP channels in thermosensation. Nature, 416(6876), 52–58. https://doi.org/10.1038/nature719
29. Dussor, G., & Cao, Y. Q. (2016). TRPM8 and migraine. Headache: The Journal of Head and Face Pain, 56(9), 1406–1417.
30. Hautakangas, H., Winsvold, B. S., Ruotsalainen, S. E., Bjornsdottir, G., Harder, A., Kogelman, L., Thomas, L. F., Noordam, R., Benner, C., Gormley, P., Artto, V., Banasik, K., Bjornsdottir, A., Boomsma, D. I., Brumpton, B. M., Burgdorf, K. S., Buring, J. E., Chalmer, M. A., de Boer, I., Dichgans, M., … Pirinen, M. (2022). Genome-wide analysis of 102,084 migraine cases identifies 123 risk loci and subtype-specific risk alleles. Nature genetics, 54(2), 152–160. https://doi.org/10.1038/s41588-021-00990-0
31. Schramm, S. H., Moebus, S., Lehmann, N., Galli, U., Obermann, M., Bock, E., Yoon, M. S., Diener, H. C., & Katsarava, Z. (2015). The association between stress and headache: A longitudinal population-based study. *Cephalalgia: an international journal of headache*, *35*(10), 853–863. https://doi.org/10.1177/0333102414563087
32. Lin, K. C., Huang, C. C., & Wu, C. C. (2007). Association between stress at work and primary headache among nursing staff in Taiwan. *Headache*, *47*(4), 576–584. https://doi.org/10.1111/j.1526-4610.2007.00759.x
33. Gillespie, N. A., Walsh, M. H. W. A., Winefield, A. H., Dua, J., & Stough, C. (2001). Occupational stress in universities: Staff perceptions of the causes, consequences and moderators of stress. *Work & stress*, *15*(1), 53–72.
34. Godwin, A., Alex, L., & Selorm, F. H. (2016). Occupational stress and its management among nurses at St. Dominic Hospital, Akwatia, Ghana. *Health Science Journal*, *10*(6), 0–0.
35. Ghorbani, A., Abtahi, S. M., Fereidan-Esfahani, M., Abtahi, S. H., Shemshaki, H., Akbari, M., & Mehrabi-Koushki, A. (2013). Prevalence and clinical characteristics of headache among medical students, Isfahan, Iran. *Journal of research in medical sciences: the official journal of Isfahan University of Medical Sciences*, *18*(Suppl 1), S24–S27.

36. Ibrahim, N. K., Alotaibi, A. K., Alhazmi, A. M., Alshehri, R. Z., Saimaldaher, R. N., & Murad, M. A. (2017). Prevalence, predictors and triggers of migraine headache among medical students and interns in King Abdulaziz University, Jeddah, Saudi Arabia. *Pakistan journal of medical sciences*, *33*(2), 270–275. https://doi.org/10.12669/pjms.332.12139
37. Yokoyama, M., Yokoyama, T., Funazu, K., Yamashita, T., Kondo, S., Hosoai, H., Yokoyama, A., & Nakamura, H. (2009). Associations between headache and stress, alcohol drinking, exercise, sleep, and comorbid health conditions in a Japanese population. The journal of headache and pain, *10*(3), 177–185. https://doi.org/10.1007/s10194-009-0113-7
38. Lin, Y.-K., Lin, G.-Y., Lee, J.-T., Lee, M.-S., Tsai, C.-K., Hsu, Y.-W., Lin, Y.-Z., Tsai, Y.-C., & Yang, F.-C. (2016). Associations Between Sleep Quality and Migraine Frequency: A Cross-Sectional Case-Control Study. Medicine, *95*(17).
39. Negro, A., Seidel, J. L., Houben, T., Yu, E. S., Rosen, I., Arreguin, A. J., Yalcin, N., Shorser-Gentile, L., Pearlman, L., Sadhegian, H., Vetrivelan, R., Chamberlin, N. L., Ayata, C., Martelletti, P., Moskowitz, M. A., & Eikermann-Haerter, K. (2020). Acute sleep deprivation enhances susceptibility to the migraine substrate cortical spreading depolarization. The Journal of Headache and Pain 2020 21:1, 21(1), 1–11. https://doi.org/10.1186/S10194-020-01155-W
40. Blau, J. N., Kell, C. A., & Sperling, J. M. (2004). Water-deprivation headache: a new headache with two variants. Headache, 44(1), 79–83. https://doi.org/10.1111/j.1526-4610.2004.04014.x
41. Price, A., & Burls, A. (2015). Increased water intake to reduce headache: learning from a critical appraisal. Journal of evaluation in clinical practice, 21(6), 1212–1218.
42. Popkin, B. M., D'Anci, K. E., & Rosenberg, I. H. (2010). Water, hydration, and health. Nutrition reviews, 68(8), 439–458.
43. Spigt, M. G., Kuijper, E. C., Schayck, C. P., Troost, J., Knipschild, P. G., Linssen, V. M., & Knottnerus, J. A. (2005). Increasing the daily water intake for the prophylactic treatment of headache: a pilot trial. European journal of neurology, 12(9), 715–718. https://doi.org/10.1111/j.1468-1331.2005.01081.x
44. Mages, S., Hensel, O., Zierz, A. M., Kraya, T., & Zierz, S. (2017). Experimental provocation of 'ice-cream headache' by ice cubes and ice water. Cephalalgia: an international journal of headache, 37(5), 464–469. https://doi.org/10.1177/0333102416650704
45. Mattsson P. (2001). Headache caused by drinking cold water is common and related to active migraine. Cephalalgia: an international journal of headache, 21(3), 230–235. https://doi.org/10.1046/j.1468-2982.2001.00211.x
46. Khorsha, F., Mirzababaei, A., Togha, M., & Mirzaei, K. (2020). Association of drinking water and migraine headache severity. Journal of clinical neuroscience: official journal of the Neurosurgical Society of Australasia, 77, 81–84. https://doi.org/10.1016/j.jocn.2020.05.034
47. Scher, A. I., Stewart, W. F., & Lipton, R. B. (2004). Caffeine as a risk factor for chronic daily headache: a population-based study. Neurology, 63(11), 2022–2027. https://doi.org/10.1212/01.wnl.0000145760.37852.ed

48. Mostofsky, E., Mittleman, M. A., Buettner, C., Li, W., & Bertisch, S. M. (2019). Prospective Cohort Study of Caffeinated Beverage Intake as a Potential Trigger of Headaches among Migraineurs. The American journal of medicine, 132(8), 984–991. https://doi.org/10.1016/j.amjmed.2019.02.015
49. Juliano, L. M., & Griffiths, R. R. (2004). A critical review of caffeine withdrawal: empirical validation of symptoms and signs, incidence, severity, and associated features. *Psychopharmacology*, *176*(1), 1–29. https://doi.org/10.1007/s00213-004-2000-x
50. Juliano, L. M., & Griffiths, R. R. (2004). A critical review of caffeine withdrawal: empirical validation of symptoms and signs, incidence, severity, and associated features. *Psychopharmacology*, *176*(1), 1–29. https://doi.org/10.1007/s00213-004-2000-x
51. Shapiro, R. E. (2008). Caffeine and headaches. Current pain and headache reports, 12(4), 311–315.
52. Lipton, R. B., Diener, H. C., Robbins, M. S., Garas, S. Y., & Patel, K. (2017). Caffeine in the management of patients with headache. The journal of headache and pain, 18(1), 107. https://doi.org/10.1186/s10194-017-0806-2
53. Hering-Hanit, R., & Gadoth, N. (2003). Caffeine-induced headache in children and adolescents. Cephalalgia: an international journal of headache, 23(5), 332–335. https://doi.org/10.1046/j.1468-2982.2003.00576.x
54. Espinosa Jovel, C. A., & Sobrino Mejía, F. E. (2017). Caffeine and headache: specific remarks. Cafeína y cefalea: consideraciones especiales. Neurologia (Barcelona, Spain), 32(6), 394–398. https://doi.org/10.1016/j.nrl.2014.12.016
55. O'Callaghan F, Muurlink O, Reid N. Effects of caffeine on sleep quality and daytime functioning. Risk Manag Healthc Policy. 2018;11:263–271.
56. Bánk, J., & Márton, S. (2000). Hungarian migraine epidemiology. *Headache*, *40*(2), 164–169. https://doi.org/10.1046/j.1526-4610.2000.00023.x
57. Abu-Salameh, I., Plakht, Y., & Ifergane, G. (2010). Migraine exacerbation during Ramadan fasting. *The journal of headache and pain*, *11*(6), 513–517. https://doi.org/10.1007/s10194-010-0242-z
58. Torelli, P., & Manzoni, G. C. (2010). Fasting headache. *Current pain and headache reports*, *14*(4), 284–291. https://doi.org/10.1007/s11916-010-0119-5
59. AlAmri, A., AlMuaigel, M., AlSheikh, M., Zeeshan, M., Suwayyid, W., & AlShamrani, F. (2021). Postprandial fasting related headache during Ramadan in Saudi Arabia: A cross-sectional study. *Cephalalgia: an international journal of headache*, *41*(11–12), 1201–1207. https://doi.org/10.1177/03331024211017915
60. Dalkara, T., & Kiliç, K. (2013). How does fasting trigger migraine? A hypothesis. *Current pain and headache reports*, *17*(10), 368. https://doi.org/10.1007/s11916-013-0368-1
61. Valderas, J. M., Starfield, B., Sibbald, B., Salisbury, C., & Roland, M. (2009). Defining comorbidity: implications for understanding health and health services. *Annals of family medicine*, *7*(4), 357–363. https://doi.org/10.1370/afm.983
62. Chang, F. Y., & Lu, C. L. (2013). Irritable bowel syndrome and migraine: bystanders or partners?. *Journal of neurogastroenterology and motility*, *19*(3), 301.

63. Lau, C. I., Lin, C. C., Chen, W. H., Wang, H. C., & Kao, C. H. (2014). Association between migraine and irritable bowel syndrome: A population-based retrospective cohort study. *European Journal of Neurology*, *21*(9), 1198–1204.
64. Mirzaei, S., Khorvash, F., Ghasemi, M., Memar-Montazerin, S., & Khazaeili, M. (2016). Migraine and irritable bowel syndrome: An epidemiological study. *Caspian Journal of Neurological Sciences*, *2*(1), 36–41.
65. Li, C., Yu, S., Li, H., Zhou, J., Liu, J., Tang, W., & Zhang, L. (2017). Clinical features and risk factors for irritable bowel syndrome in migraine patients. *Pakistan Journal of Medical Sciences*, *33*(3), 720.
66. Kawashima, K., Fukuba, N., Uemura, Y., Ota, K., Kazumori, H., Sonoyama, H., Oka, A., Tada, Y., Mishima, Y., Oshima, N., Yuki, T., Katsube, T., Kinoshita, Y., & Ishihara, S. (2020). Comorbid irritable bowel syndrome symptoms and headache have greater association with anxiety than depression: Annual health check-up survey results. *Medicine*, *99*(47), e23059. https://doi.org/10.1097/MD.0000000000023059
67. Grover, M., Kolla, B. P., Pamarthy, R., Mansukhani, M. P., Breen-Lyles, M., He, J. P., & Merikangas, K. R. (2021). Psychological, physical, and sleep comorbidities and functional impairment in irritable bowel syndrome: Results from a national survey of US adults. *PloS one*, *16*(1), e0245323.
68. Arzani, M., Jahromi, S. R., Ghorbani, Z., Vahabizad, F., Martelletti, P., Ghaemi, A., Sacco, S., Togha, M., & School of Advanced Studies of the European Headache Federation (EHF-SAS) (2020). Gut-brain Axis and migraine headache: a comprehensive review. *The journal of headache and pain*, *21*(1), 15. https://doi.org/10.1186/s10194-020-1078-9
69. Camilleri M. (2009). Serotonin in the gastrointestinal tract. *Current opinion in endocrinology, diabetes, and obesity*, *16*(1), 53–59. https://doi.org/10.1097/med.0b013e32831e9c8e
70. Schürks, M., Rist, P. M., & Kurth, T. (2010). 5-HTTLPR polymorphism in the serotonin transporter gene and migraine: a systematic review and meta-analysis. *Cephalalgia: an international journal of headache*, *30*(11), 1296–1305. https://doi.org/10.1177/0333102410362929
71. Zhang, Z. F., Duan, Z. J., Wang, L. X., Yang, D., Zhao, G., & Zhang, L. (2014). The serotonin transporter gene polymorphism (5-HTTLPR) and irritable bowel syndrome: a meta-analysis of 25 studies. *BMC gastroenterology*, *14*, 23. https://doi.org/10.1186/1471-230X-14-23
72. Glintborg, D., Hass Rubin, K., Nybo, M., Abrahamsen, B., & Andersen, M. (2015). Morbidity and medicine prescriptions in a nationwide Danish population of patients diagnosed with polycystic ovary syndrome. *European journal of endocrinology*, *172*(5), 627–638. https://doi.org/10.1530/EJE-14-1108
73. BANDAY, M., WANI, M., FAROOQ, U., PARRA, B., & RATHER, Y. (2020). Sociodemographic and comorbidity profiles of migraine patients: an outpatient-based study in a tertiary care hospital. *Asian Journal of Pharmaceutical and Clinical Research*, 59–64.
74. Kujanpää, L., Arffman, R. K., Pesonen, P., Korhonen, E., Karjula, S., Järvelin, M. R., Franks, S., Tapanainen, J. S., Morin-Papunen, L., & Piltonen, T. T. (2022). Women with polycystic ovary syndrome are burdened with multimorbidity and medication use independent of body mass index at late fertile

age: A population-based cohort study. *Acta obstetricia et gynecologica Scandinavica*, *101*(7), 728–736. https://doi.org/10.1111/aogs.14382

75. Ramly, B., Afiqah-Aleng, N., & Mohamed-Hussein, Z. A. (2019). Protein-Protein Interaction Network Analysis Reveals Several Diseases Highly Associated with Polycystic Ovarian Syndrome. *International journal of molecular sciences*, *20*(12), 2959. https://doi.org/10.3390/ijms20122959
76. Muayqil, T., Al-Jafen, B. N., Al-Saaran, Z., Al-Shammari, M., Alkthiry, A., Muhammad, W. S., Murshid, R., & Alanazy, M. H. (2018). Migraine and Headache Prevalence and Associated Comorbidities in a Large Saudi Sample. *European neurology*, *79*(3–4), 126–134. https://doi.org/10.1159/000487317
77. Caponnetto, V., Deodato, M., Robotti, M., Koutsokera, M., Pozzilli, V., Galati, C., Nocera, G., De Matteis, E., De Vanna, G., Fellini, E., Halili, G., Martinelli, D., Nalli, G., Serratore, S., Tramacere, I., Martelletti, P., Raggi, A., & European Headache Federation School of Advanced Studies (EHF-SAS) (2021). Comorbidities of primary headache disorders: a literature review with meta-analysis. *The journal of headache and pain*, *22*(1), 71. https://doi.org/10.1186/s10194-021-01281-z
78. Togha, M., Karimitafti, M. J., Ghorbani, Z., Farham, F., Naderi-Behdani, F., Nasergivehchi, S., … Jafari, E. (2022). Characteristics and comorbidities of headache in patients over 50 years of age: a cross-sectional study. *BMC geriatrics*, *22*(1), 1–10.
79. Yazar, T., Yazar, H. O., Aygün, A., Karabacak, V., Altunkaynak, Y., & Kirbaş, D. (2021). Evaluation of serum uric levels in migraine. *Neurological sciences: official journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology*, *42*(2), 705–709. https://doi.org/10.1007/s10072-020-04598-w
80. Lima Carvalho, M. F., de Medeiros, J. S., & Valença, M. M. (2017). Headache in recent onset hypothyroidism: Prevalence, characteristics and outcome after treatment with levothyroxine. *Cephalalgia: an international journal of headache*, *37*(10), 938–946. https://doi.org/10.1177/0333102416658714
81. Rubino, E., Rainero, I., Garino, F., Vicentini, C., Govone, F., Vacca, A., Gai, A., Gentile, S., Govone, G., Ragazzoni, F., Pinessi, L., Giordana, M. T., & Limone, P. (2019). Subclinical hypothyroidism is associated with migraine: A case-control study. *Cephalalgia: an international journal of headache*, *39*(1), 15–20. https://doi.org/10.1177/0333102418769917
82. Spanou, I., Bougea, A., Liakakis, G., Rizonaki, K., Anagnostou, E., Duntas, L., & Kararizou, E. (2019). Relationship of Migraine and Tension-Type Headache With Hypothyroidism: A Literature Review. *Headache*, *59*(8), 1174–1186. https://doi.org/10.1111/head.13600
83. Trauninger, A., Leél-Ossy, E., Kamson, D. O., Pótó, L., Aradi, M., Kövér, F., Imre, M., Komáromy, H., Erdélyi-Botor, S., Patzkó, A., & Pfund, Z. (2011). Risk factors of migraine-related brain white matter hyperintensities: an investigation of 186 patients. *The journal of headache and pain*, *12*(1), 97–103. https://doi.org/10.1007/s10194-011-0299-3
84. Lauritzen, M., & Strong, A. J. (2001). Evidence for CSD or CSD-Like Phenomena in Human Brain in Relation to Migraine and Stroke. Ischemic Blood Flow in the Brain, 335–342. https://doi.org/10.1007/978-4-431-67899-1_41

85. Mansouri, M., Sharifi, F., Varmaghani, M., Yaghubi, H., Shokri, A., Moghadas-Tabrizi, Y., Keshtkar, A., & Sadeghi, O. (2020). Dairy consumption in relation to primary headaches among a large population of university students: The MEPHASOUS study. *Complementary therapies in medicine*, *48*, 102269. https://doi.org/10.1016/j.ctim.2019.102269
86. Nazari, F., & Eghbali, M. (2012). Migraine and its relationship with dietary habits in women. *Iranian journal of nursing and midwifery research*, *17*(2 Suppl 1), S65–S71.
87. Rist, P. M., Buring, J. E., & Kurth, T. (2015). Dietary patterns according to headache and migraine status: a cross-sectional study. *Cephalalgia: an international journal of headache*, *35*(9), 767–775. https://doi.org/10.1177/0333102414560634

Figures

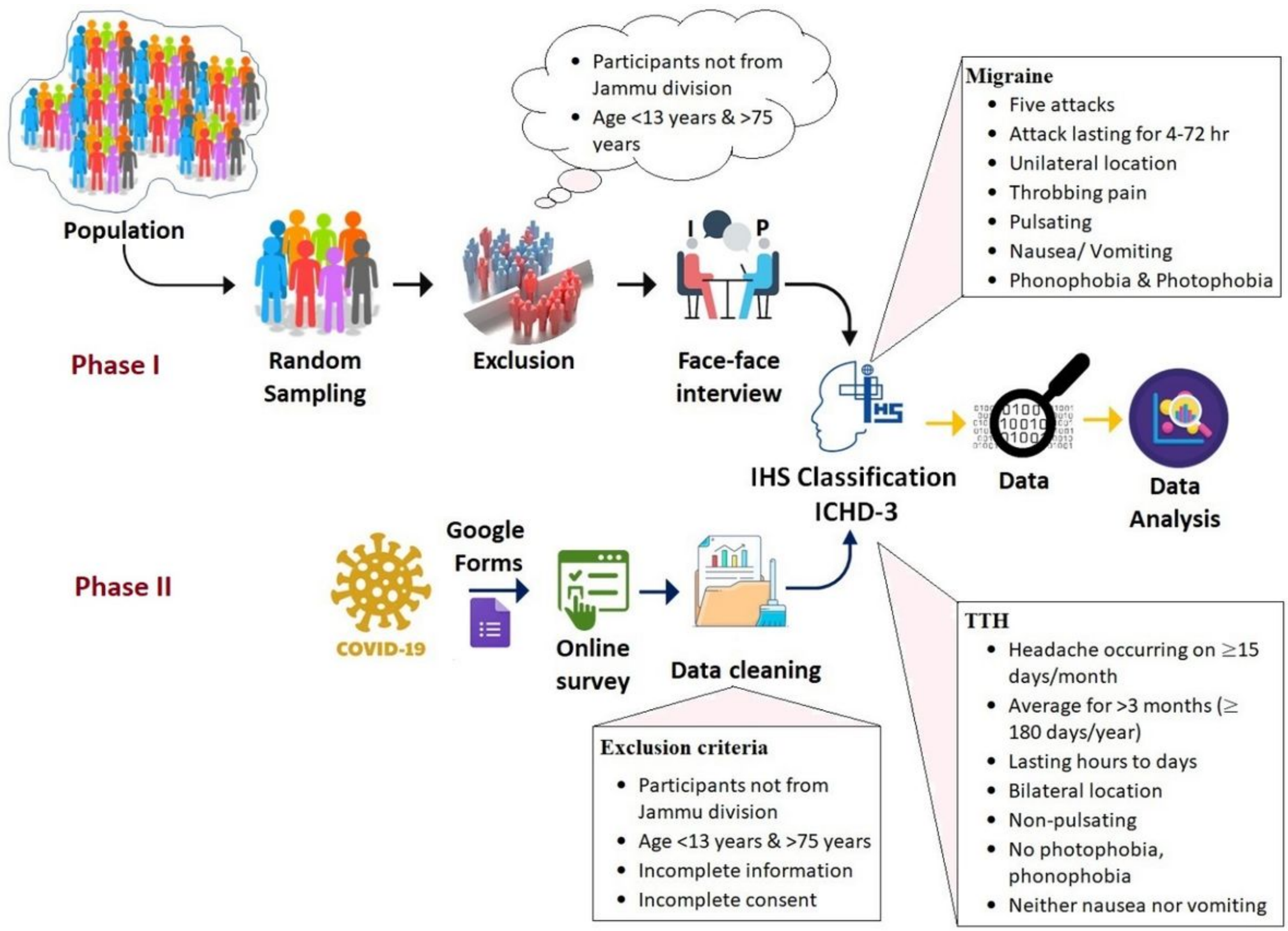

Figure 1

Pictorial representation of the data collection in the present survey

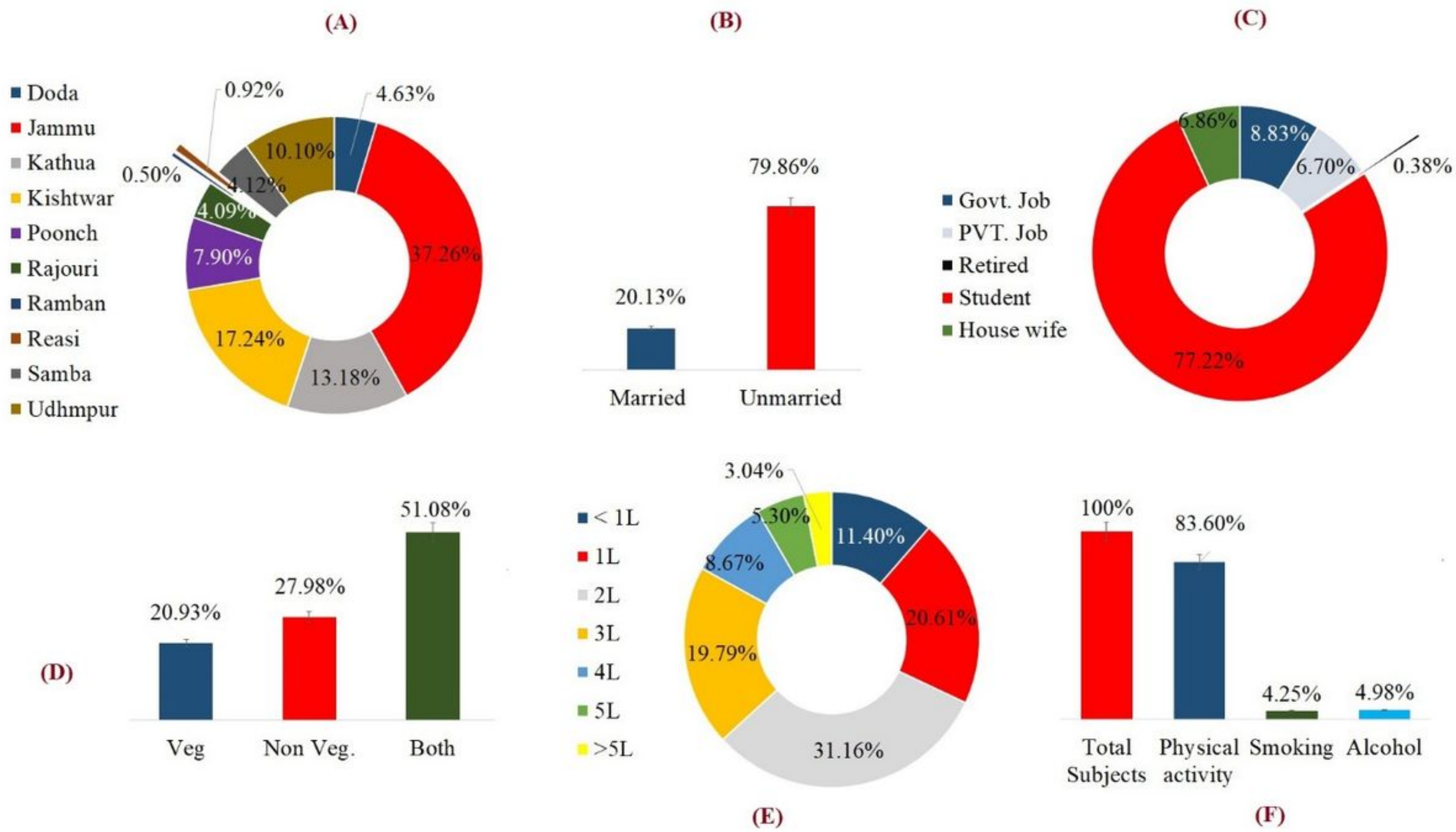

Figure 2

Demographic infographics: (A): Doughnut representing the total subject inclusion from the different parts of the Jammu division **(B):** Column graph showing the martial status, **(C):** Doughnut graph represent the occupation status of participants, **(D):** Dietary habit of the participants, **(E):** Doughnut diagram shows the frequency of the total water intake in liter by the participants. **(F):** Presentation of frequency of different data variable such as “physical activities”, “smoking”, & “alcohol usage”.

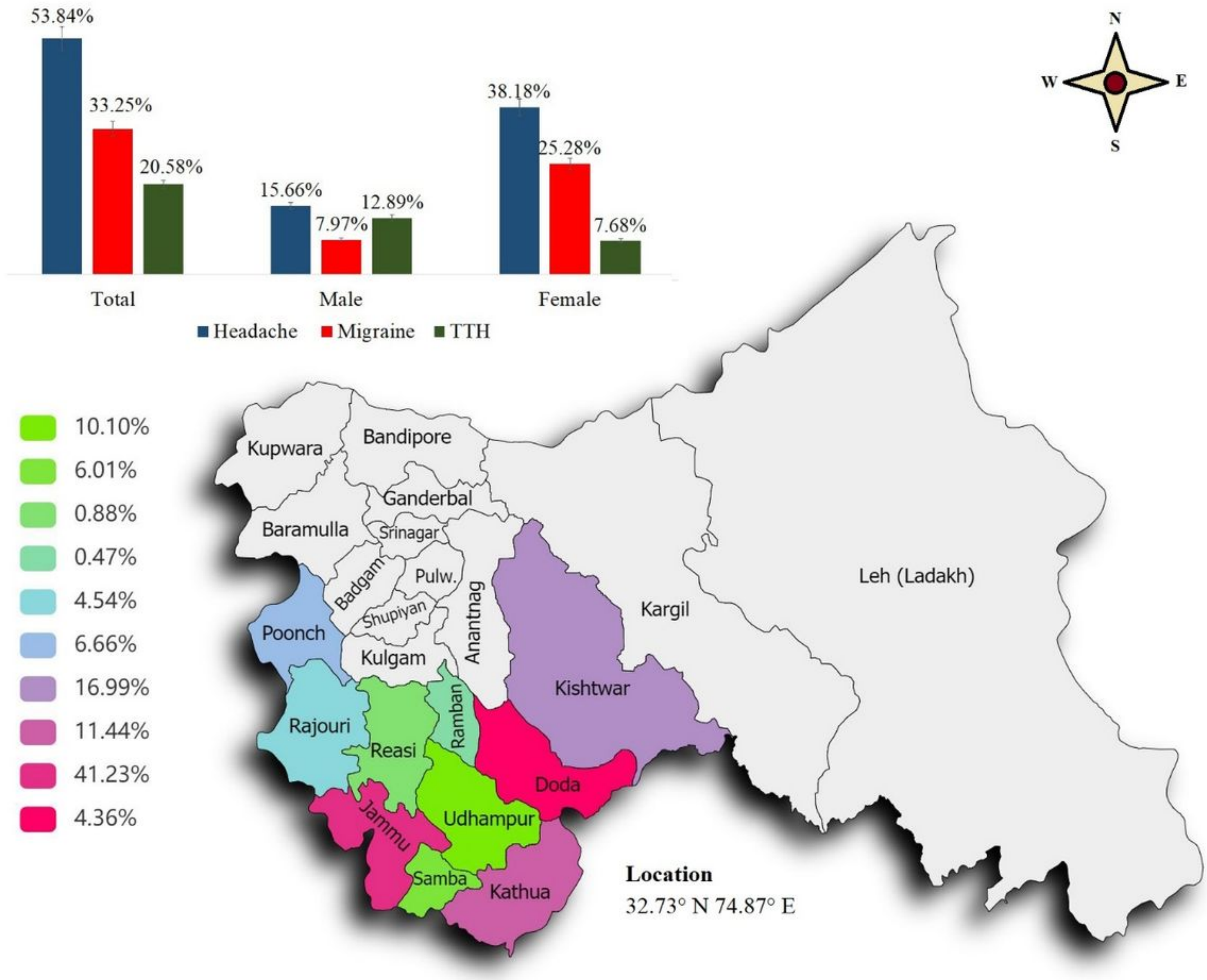

Figure 3

Prevalence of Headache in the Jammu region of north Indian population

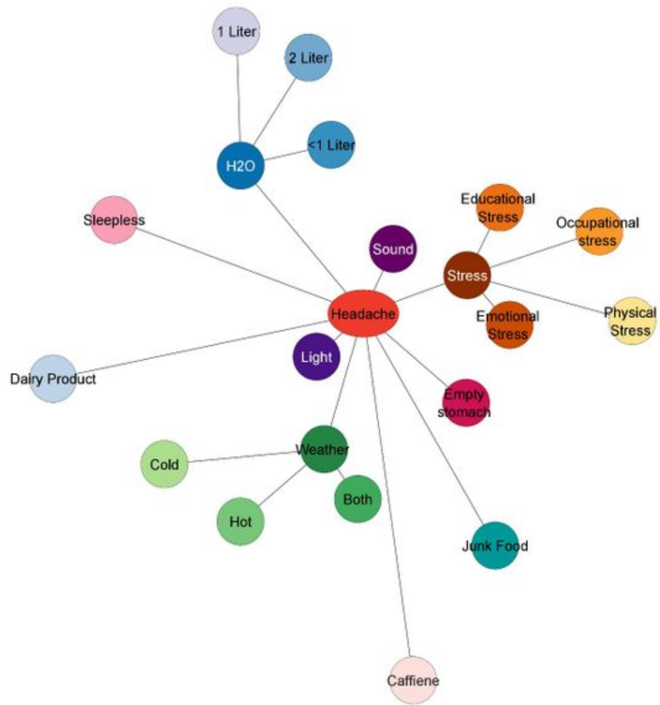

Figure 4

Environmental risk factor association: [Cytoscape 3.9.2: Weighted network based on measure of strength of association i.e., Odds Ratio: Edges are defined by the OR values depicting the association between different peripheral node and the core node].

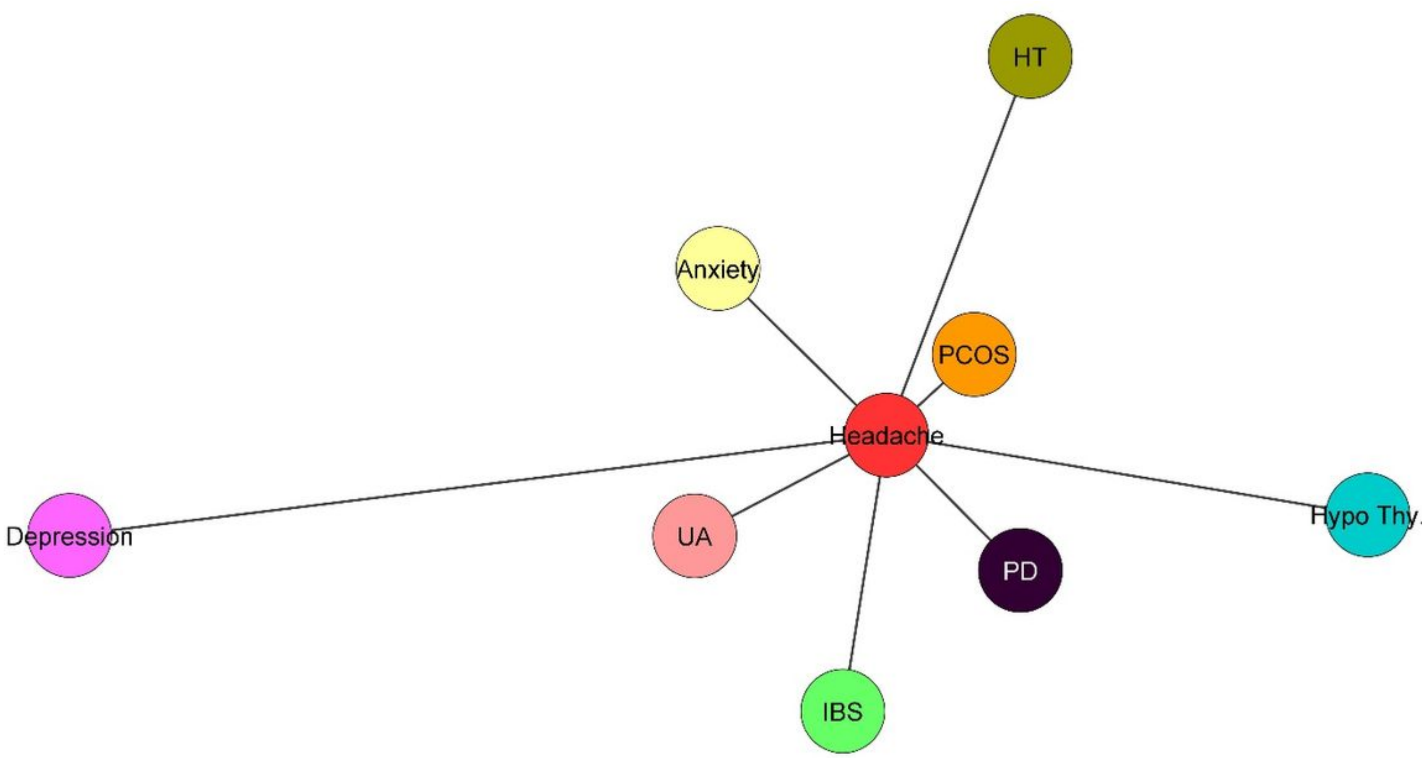

Figure 5

Comorbidity Weighted association graph: Hypo Thy (Hypothyroidism). OR: 2.5886, 95% CIs [1.0248-6.5386] (p=0.0442), **IBS** (Irritable Bowel Syndrome) OR: 3.8084, 95% [1.7610-8.2360] (p=0.0007), **PCOS** (Poly cystic Ovarian Syndrome) OR: 8.6336, 95% CIs [3.9528-18.8570] (p<0.0001), **Anxiety** OR: 4.5373, 95% CIs [3.9000-5.2787] (p<0.0001), Hypertension **(HT)** OR: 2.9246, 95% CIs [1.9785-4.3231] (p<0.0001), Depression OR: 1.9363, 95% CIs [1.1651-3.2181] (p=0.0108), Panic disorder **(PD)** OR: 5.0411, 95% CIs [1.9463-3.0570] (p=0.0009), Uric acid **(UA)** OR: 4.7390, 95% CIs [1.0487-2.14158] (p=0.0432) **[Cytoscape 3.9.2: Weighted network based on measure of strength of association i.e., Odds Ratio: Edges are defined by the OR values depicting the association between different peripheral node (Disorder) and the core node i.e., Headache].**

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Visualabstarctfinal.jpg