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## Editorial Thanks: IHRJ Completes Three Years of Successful Publication

IHRJ Editorial Team

*Dear readers and authors,*

It is an immense pleasure to inform you that the current issue is the 36<sup>th</sup> Issue in the glorious publishing history of IHRJ, and we have completed three years of providing an international global platform to all our authors and readers to publish, read and disseminate scientific knowledge.

The editorial board wishes your safety during these testing times of the COVID-19 Pandemic. We urge you all to follow basic hygiene measures like washing your hands every 20 minutes and sneezing on your closed elbow, etc.

There is no need to panic and do follow WHO and CDC guidelines for the prevention of COVID-19.

Stay safe and educate others regarding their safety to prevent the COVID-19 pandemic.

The entire idea of IHRJ was born when the editor and co-editor decided to provide a platform to the researchers that is quick to answer their queries and be there for researchers at all time. And thus, after brainstorming for a lot of names, International Healthcare Research Journal (IHRJ) was agreed upon.

After this, the main work began. While the co-editor began working on the website design, the editor started to gather a team of dedicated researchers and clinicians to be member of the national and international editorial board. The first issue was released on 12<sup>th</sup> April, 2017 and we applied for our ISSN number, initiating the series of indexings and constant upgradation of the journal based on the response of our users.

**In the span of 36 months, we have covered a lot of ground and our humble achievements are:**

1. NLM cataloged journal within 6 months of launch.
2. Shifting from a normal website to OJS 3.0 with a dedicated journal management system for further transparency and convenience of our authors which

is based on global standards.

3. Proudly partnering for the 5<sup>th</sup> Medical Tourism Annual Conference, held on the 13<sup>th</sup> and 14<sup>th</sup> of March 2019 in Zagreb, Croatia.

4. Publications from various countries: Saudi Arabia, Nepal, USA, Ivory Coast, Madagascar, Sudan, Nigeria, Canada, etc.

5. Partial sponsor for the 25<sup>th</sup> National IAPHD conference held at Modinagar (2018).

6. Plagiarism free manuscripts.

7. DOI number generated for every article.

8. Round the clock support to our authors.

9. HTML, EPUB and MOBI files generated of articles after October 2018.

10. Starting April 2019, the journal website is SSL certified, making it more secure.

11. Inclusion in Index Copernicus, Europub and BASE

12. Submission of all metadata to OAI-PMH, Zenodo, Crossref and Index Copernicus.

13. Welcoming onboard newer reviews and editorial board members

14. A total of 235 manuscripts have been published from April 2017- 31<sup>st</sup> December, 2019.

15. We have also published a total of 1086 pages of scientific literature.

### Future Plans

1. IHRJ aims to visit at least one international conference every year for increasing the reach of the journal.

2. Indexing in various agencies.
3. Hiring more staff to handle the increased flow of manuscripts.

The journey for IHRJ has just started. We thank those who have believed in us for it's because of them that IHRJ has come so far.....

*"No Road is long...  
When Dreams are BIG...  
And Sky is the limit...."*  
-Anonymous

We seek your continued support as we start with our 4<sup>th</sup> Volume scheduled to be published on or before 25<sup>th</sup> April, 2020.

**With Thanks and Regards,**  
Editorial Team  
International Healthcare Research Journal (IHRJ).



# EVALI: A Review of the Vaping Related Lung Injury

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Vaping or e-cigarettes were introduced to help people quit smoking tobacco but with every passing year, their demand has dramatically increased as compared to the traditional cigarettes. With the increase in the number of vapers, an alarming vaping related outbreak which was given an official name by the CDC: EVALI (Electronic cigarette or Vaping Product Associated Lung Injury). In the United States, until January 21<sup>st</sup>, 2020 2051 cases have been reported from all 50 states with 60 deaths confirmed in 27 states and the district of Columbia. Not much is known about the cause of this outbreak but the possible culprits could be THC(Tetrahydrocannabinol) containing materials or Vitamin E Acetate. In order to protect the youth and the adults from such health hazards the government took a step by putting a ban on E-cigarettes. After the US states of Michigan & New York, India too, imposed a ban on the sale of such e-cigarettes. This review paper discusses about e-cigarettes and about its harmful effects that lead to EVALI in a person.

**KEYWORDS:** E-cigarettes, Vaping, Smoking Cessation, ENDS

## INTRODUCTION

Meant to be safer, harmless and having no-tobacco, the Electronic cigarette (e-cigarette) was first patented in 1967 by Herbert A. Gilbert from Beaver Falls, PA.<sup>1</sup> They gained immense popularity after a Chinese pharmacist named Hon Lik introduced e-cigarettes in the Chinese market through his employer in 2004 and ever since, are freely available over the internet for users to buy and use.<sup>2</sup>

These (e-cigarettes) are also commonly known as Electronic Nicotine Delivery Systems (ENDS) and is a product which is operated through a battery which helps deliver nicotine through inhalable aerosol generated from a nicotine-containing solution. The term “vaping” is associated with an e-cigarette use. Vaping is finding an increase in its use, especially among the young population as it gives a sensation as well as provides the same taste and feeling of inhaling smoke that mimicking smoking from paper cigarettes. Not just e-cigarettes, but vape pens and advanced personal vaporisers (MODS) too are the devices used for vaping.

They were initially used as an alternative to regular smoking and were initially considered safe to use. However, the health consequences, arising from the long-term use of these e-cigarettes, i.e. (1) Its efficacy as

compared to combustible cigarette smokers to help them to reduce and/or stop smoking, (2) The extent of carcinogens in e-cigarettes and, (3) the role of these products in initiating and perpetuating nicotine dependence in teenagers and young adults has been debated constantly across the globe.<sup>3</sup>

There have been various cases reported of lung injury as a result of these e-cigarettes and in this context, on October 11<sup>th</sup>, 2019,<sup>4</sup> The Centres for Disease Control and Prevention (CDC) in its morbidity and mortality weekly report issued have given an official name to the vaping related illness named: EVALI (E-cigarette or Vaping Product Associated Lung Injury). This review paper discusses about e-cigarettes and about its harmful effects that lead to EVALI in a person.

## WHAT IS AN E- CIGARETTE?

An E- cigarette is a hand held powered vaporizer which includes hand to mouth action of smoking but without combustion of tobacco and are categorised in to three groups: disposable, rechargeable and modular.<sup>5</sup> They have a battery powered vaporizer that uses a heating element to heat e-liquid, typically containing nicotine, from a cartridge that produces a chemical filled aerosol. The effectiveness of an e-cigarettes depends on a variety of factors which include battery strength, the nature of



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the circuit used, solutions/flavour used and the user's smoking behaviour, among others. Since they work by producing vapours, their effectiveness has a direct dependence on the product's competence to heat the solution into a state where it transforms into vapour. As a result, the battery's voltage and circuit strength are also crucial components. The stronger the voltage and circuit, faster will the solution heat up and vaporise, and more effective will be the product. Electronic Smoking Device aerosol (ESD) that operate using a single coil heating element produce much higher levels of toxins at higher temperatures than double-coil devices across different e-liquids that produce aerosol at lower temperatures.<sup>6</sup>

E-cigarettes contain nicotine cartridges with airflow sensors, but do not burn tobacco.<sup>7</sup> Many e-liquids or e-juice comes in fruit flavours, making them appealing to kids. There are over 466 brands and 7764 unique flavours with about 242 new flavours added per month.<sup>8</sup> Instead of cigarette smoke, the user inhales as an aerosol, commonly called vapour.<sup>9</sup>

### MARKET SHARE OF VAPE PRODUCTS

As per a report, the number of vapers have alarmingly increased from 7 million (2011) to 41 million (2018). The FDA in 2018 reported that approximately 3.62 million students users belonged to middle and high schools in the USA itself. With a span of one year, the current e-cigarette use (use on at least one day in the past 30 days) in the same study population increased from 11.7 to 20.8 percent.<sup>10</sup>

It has also been estimated that the number of adults who vape will reach almost 55 million by the year 2021 and the global market currently is estimated to be worth \$19.3 bn which is approximately three times higher as compared to \$6.9 bn five years ago. USA has the largest market share of vape products followed closely by UK. Market estimates have suggested that in 2014, there were at least 466 brands producing e-cigarettes and by 2030 the global e-cigarette market would rise by 17 times.

### MARKET SHARE IN INDIA

India has more than ten 100 million adult smokers, making it a huge lucrative and a potential market for e-cigarette companies. A single disposable e-cigarettes ranges from \$6 to \$12 (INR 390-782) and the cartridge models are rechargeable and contain pre-filled cartridges starter kits, which usually range around \$40 to \$ 60 (INR 2600-3900).<sup>12</sup> In India, there are 75

companies that were supplying these e-cigarettes on line. During 2015-16 to 2018-19 e-cigarettes worth \$1,91,781 were imported in India which were mostly imported from China, US, Hong Kong and Germany.

### EVALI: THE PROBABLE CULPRITS

To educate vapers, Dr. Stanton Glantz, Director for the Center for Tobacco Control Research and Education at the University of California, San Francisco stated that *"If you are somebody who is using an e-cigarette, you are breathing an aerosol of exhaled nicotine, ultra fine particles, volatile organic compounds and other toxins"*.<sup>14</sup>

An Electronic Smoking Device aerosol (ESD) is made up of high concentration of ultrafine particles and the particle concentration is higher than in conventional tobacco cigarette smoke.<sup>13</sup> Exposure to fine and ultrafine particles may exacerbate respiratory ailments like asthma and constrict arteries which could trigger a heart attack.<sup>14</sup> The compounds that have been identified in mainstream (MS) or second hand (SS) ESD aerosol include: Acetaldehyde(MS), Benzene(SS), Cadmium(MS), Formaldehyde(MS,SS), Isoprene(SS), Lead (MS), Nickel(MS), Nicotine (MS,SS), N-Nitrosornicotin (MS,SS) and Toluene(MS,SS). Short term exposure of propylene glycol a chemical that is used as a base in ESD solution and is one of the primary component in aerosol emitted by ESD causes eye, throat and airway irritation, whereas long term exposure can result in children developing asthma.<sup>15</sup>

Henderson TR et al. (1981)<sup>16</sup> reported that heating propylene glycol changes its chemical composition and produces small amount of propylene oxide, a known carcinogen. Detectable levels of nitrosamines, diethylene glycol, glycerol, propanal, diactin and triactine have been reported in ESD aerosol.<sup>17,18</sup> Short term use of ESD has been shown to increase respiratory resistance and impair lung function, which may result in difficult breathing<sup>19</sup> reported that ESD exposure especially to cinnamon damages lung tissues due to increased oxidative stress and inflammatory responses. Toxic chemicals attached to nanoparticles in ESD aerosol that are much smaller than the particle size in tobacco have adverse health effects than when these toxins are attached to large tobacco smoke particles.<sup>20</sup>

### CAUSES OF EVALI

Since not much is known about the real cause of EVALI right now, it is believed that it might be an overlap with smoking related injuries or it might be a completely different phenomenon. However, the only difference

was that many of the individuals who reported with the condition exclusively used vaping products and were not smoking the conventional cigarettes.

Officials at the CDC said that THC (Tetrahydrocannabinol) containing products may be behind this outbreak in lung illness related to vaping. THC is the key psychoactive compound that is found in marijuana which in turn is responsible for the feeling of being high. Around 16 percent of the sick patients claimed that they had used products that contained nicotine but not THC whereas 77 percent claimed of using products containing a mix of both.<sup>21</sup> The CDC even has reported that these THC – containing products were obtained from informal sources like friends, family, or directly from the drug dealers (in Illinois and Wisconsin).

Another possible culprit that the CDC believes, which could be responsible for such chemical exposure rather than an infection has been identified as Vitamin E acetate.<sup>21</sup> Vitamin E acetate is a nutritional supplement that can be ingested as a vitamin supplement, or applied to the skin and is not known of causing any harm, however it is not approved as a vaping additive by New York State Medical Marijuana Program. The New York State Department of Health, after its thorough investigation stated that nearly all cannabis containing samples contained very high levels of this compound and no such traces were found in nicotine containing samples.<sup>21</sup> CDC is keeping an eye and still investigating the oil like compound which could be a possible culprit of EVALI.

### CASES REPORTED OF EVALI

CDC, U.S Food and Drug administration (FDA), all state and the local health departments, and other clinical and public health sectors are investigating a multistate outbreak of the lung injury associated with e-cigarette, or vaping products. January 21<sup>st</sup>, 2020 2051 cases have been reported from all 50 states with 60 deaths confirmed in 27 states and the district of Columbia. Such an increase in the number of cases as well as mortality is the reason that CDC and other governmental agencies are directing their effort to prevent EVALI by either banning the ENDS or educating the public regarding the harmful effects of vaping.

As per CDC, approximately 90 percent of the cases that were reported with symptoms were hospitalized and many of them required supplemental oxygen, few of

them had to be put on ventilator to help breathe while many had to be put on corticosteroids to reduce the lung inflammation. The cases reported with the signs and symptoms such as coughing, shortness of breath, nausea, fatigue, weight, night sweats, low oxygen levels, and hazy spots on a lung X-ray.<sup>22</sup> Such developments can be of extreme concern as most of the cases reported included teenagers or young adults. Some cases were characterised by pneumonitis (lung inflammation), some with accumulation of oil in the lungs, while others involved accumulation of white blood cells.<sup>23</sup>

### INDIAN SCENARIO

In India till date no cases have been reported of EVALI, but that does not signify that the people of India who have been vaping are under no threat of developing the signs and symptoms of EVALI. The use of e-cigarettes prior to the ban by the population was increasing day by day and is it quite possible that the subjects reporting with symptoms could have been underreported by the patients to their attending doctors, or could have simply been associated with combustible tobacco use. The presence of air pollution could have also been a confounding factor (Especially in metropolitan areas where the AQIs are quite higher) in the proper diagnosis of EVALI and hence, no such cases have been reported till date.

### MEASURES TAKEN

CDC is working day and night to identify the cause of the outbreak in collaboration with the states and other federal agencies. They even have activated the Emergency Operations Centre (EOC) to coordinate activities and to provide help to states, public health partners as well as the clinicians around the nation. By invitation the Epidemic Intelligence Service (EIS) officers and other CDC staff has been deployed by CDC. Few other range of laboratory investigation made possible by CDC and FDA include:

- Testing bronchoalveolar lavage (BAL) fluid samples along with the urine and blood samples paired to BAL fluid samples.
- Testing the pathological samples, that includes lung biopsy or autopsy specimen.
- Aerosol emission testing which will augment the ongoing work of FDA to characterize e-liquid and help in better understanding of the lung injury breakout.
- Apart from several laboratory investigations, Ban on the use of e-cigarette or other vaping products too have been imposed in several states globally. In the US,

Michigan has become the first state to impose ban on flavoured e-cigarettes, with New York being the second state to impose the ban.

## INDIA

A day after New York's ban, Modi government on 18<sup>th</sup> September, 2019 too announced a ban on e-cigarettes confirming the health risks they pose to the youth and the increasing addiction to be alarming.<sup>24</sup> The government said, the main aim to ban e-cigarettes was protecting the youth, the section of the society which is most vulnerable to addiction and its health hazards. 15 states and one union territory prior to any announcement being made, had already banned e-cigarette which include, Punjab, Karnataka, Mizoram, Kerala, Jammu & Kashmir, Uttar Pradesh, Bihar, Maharashtra, Tamil Nadu, Jharkhand, Himachal Pradesh, Pondicherry, Rajasthan, Meghalaya, Odisha, and Nagaland.

## FINES UNDER THE NEW LAW (INDIA)

Once the law passed in 2019 comes into effect, certain provisions will be made applicable.<sup>23</sup> The production, manufacture, import, export of e-cigarettes shall become an identifiable offence in India, which will be punished with an imprisonment of up to one year or fine up to 1 lakh or both for the first offence.

- The punishment of imprisonment up to 3 years and fine up to 5 lac, if someone caught disobeying the law again.
- Punishment of imprisonment up to 6 months or fine up to Rs 50,000 for those found storing e-cigarettes.
- The dealers that have existing stocks of e- cigarettes need to inform the nearest police station on their own before strict actions are taken against them.

## VAPING: AN ETHICAL DILEMMA

e-cigarettes in the first place were introduced to help people quit smoking tobacco. However, there are no such studies that show vaping actually helps people quit smoking. In 2015, U.S surgeon general reported a hike in consumption of E-cigarette by 900%, in which 40% users had never smoked the traditional cigarette. The traditional as well the E -cigarette, both contain nicotine and can be equally addictive as cocaine or heroin. In fact, few of the e-cigarette users get more nicotine than the traditional ones as, extra strength cartridges are available which have a higher concentration of nicotine or a higher hit of the substance can be achieved by increasing the voltage of E - cigarette. Vaping is definitely less harmful than

smoking the traditional cigarette, but still it is not safe. Hence electronic cigarettes are not the best smoking cessation tools.

## PREVENTION OF EVALI

As vitamin E-Acetate is listed as a possible culprit of EVALI, but evidence is not yet so substantial to rule out the contribution of other chemicals that are present in an E- Cigarette. Till then the CDC recommends all the people to consider refraining themselves from using E - Cigarette or vaping, products. THC used very often has also been associated as another probable cause of EVALI, so the people are recommended not to use THC containing E- Cigarettes, vapes, or other products in order to avoid any harmful effects it may pose. Population with Marijuana use disorder should seek medical help as it has other ill effects as well. Adults who are not tobacco consumers yet, should not start using E-Cigarette as they might consider it to be less harmful which is a persistent ethical dilemma in our society. Adults who continue to use E-cigarettes should keenly monitor themselves for any sort of symptoms and get the symptoms checked by a health care provider, if any resemblance found with those reported in the outbreak.

Adults using E-Cigarette as tobacco cessation method, trying to quit smoking are recommended to quit this habit and not going back to smoking the conventional ones rather considering using FDA approved nicotine replacement therapies.

## CONCLUSION

With the CDC giving a name to the vaping related lung injuries, maximum-impact mass awareness programs need to be undertaken across the globe. Other countries should also report such cases so that significant conclusions regarding its aetiology and management can be established. If a complete ban is not feasible, a health warning among the packs should be made mandatory and any new flavour/product should only be introduced with necessary regulatory approvals so that the mortality and mortality associated with EVALI can be decreased.

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# Drug Related Hypertension: A Review on an Unappreciated Cause of Blood Pressure Increase

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Blood pressure elevation is known to be a determining risk factor for cardiovascular disease and mortality. Although blood pressure increase has many causative factors, numerous drugs have also been reported to increase blood pressure. Drugs are often overlooked as a reason of hypertension. A few medications that usually help to reduce blood pressure may increase blood pressure paradoxically or may lead to blood pressure elevation on discontinuation due to a rebound effect. Detailed evaluation of patient's medical therapy may help to identify the culprit drug. Discontinuation of the causative agent is recommended once the drug induced hypertension has been identified. The present review summarizes the therapeutic agents that can induce hypertension and would allow the clinician to recognize this entity and to take the appropriate therapeutic measures.

**KEYWORDS:** Hypertension, Blood Pressure, Glucocorticoids

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## INTRODUCTION

Rapid diagnosis of hypertension can help prevent serious complications such as intracranial bleeding and heart failure. Identification of the intake of these substances may be important because their elimination can obviate the need for unnecessary, costly, and potentially dangerous evaluations, treatments, or both.<sup>1</sup> Drugs are often overlooked either as a cause of hypertension or as a cause of BP destabilization. Therefore, it is necessary to pay attention to the patient's pharmacological medical history, identify possible drug causes and subsequently evaluate the relevance of the adverse events. Drug related elevation of blood pressure can be caused by various mechanisms including increased intravascular volume due to inadequate hydration or fluid retention, direct or indirect activation of the sympathetic nervous system, direct vascular influence - vasoconstriction.<sup>2</sup>

Drugs that can increase BP include antidepressants, glucocorticoids, thyroid hormones, immunosuppressants, or drugs that lead to mineralocorticoid excess by their mechanism, non-steroidal anti-inflammatory drugs and sex hormones. Special attention should also be paid to blood pressure elevations during treatment with angiogenesis inhibitors in cancer patients.<sup>3</sup>

## ANTI-DEPRESSANT DRUGS

The effect on blood pressure depends on which mediators and receptors are affected by the antidepressant and the dose of administered drug. Blood pressure elevation is probably caused by their noradrenergic effect.<sup>2</sup> Tricyclic antidepressants can result in hypertension by affecting noradrenaline and serotonin reuptake, and have other effects such as anticholinergic, antihistamine and alpha-1 lytic, which modulate the overall impact on the cardiovascular system and on the resulting blood pressure. The magnitude of the antidepressant dose administered is important in assessing the association of hypertension with the medication. For amitriptyline, dosulepine, clomipramine and maprotiline hypertension is not reported as an adverse reaction at all, for nortriptyline, the incidence rate of hypertension is reported as an uncommon adverse side effect, and for imipramine, the incidence rate of hypertension is reported as very rare.<sup>4</sup>

The risk of BP elevation and tachycardia when mirtazapine is administered is very low; the probability of occurrence lower than 50% compared to tricyclic antidepressants is stated.<sup>5</sup> High doses of venlafaxine cause hypertension in more than 12% of patients. A meta-analysis has shown that BP increase is more



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pronounced in the elderly and in male patients and is dose dependent.<sup>5</sup> The incidence of elevated diastolic BP > 90 mmHg was statistically and clinically significant only at doses above 300 mg of venlafaxine per day.<sup>6</sup>

### ANTINEOPLASTIC AGENTS

Hypertension is a common side effect that occurs during treatment with agents blocking the vascular endothelial growth factor pathway. These include monoclonal antibodies and tyrosine kinase inhibitors. Binding of VEGF to the respective receptor leads to activation of tyrosine kinase. VEGFR<sub>1</sub> and VEGFR<sub>2</sub> are mainly localized in endothelial cells. Activation of VEGFR<sub>2</sub> triggers regulatory pathways necessary for endothelial biology. The stimulation of phospholipase C and its associated cascades, which play an important role in cell growth and differentiation, represent the first pathway. The second route leads to activation of phosphatidylinositol-3 kinase - protein kinase B, phosphorylation of endothelial nitric oxide synthase, increased production of nitric oxide and subsequent vasodilation. Third, VEGFR<sub>2</sub>-mediated activation of cyclooxygenase stimulates the production of vasodilatory prostacyclin.<sup>7,8</sup> Another route involving cytoplasmic tyrosine kinases influences adhesion and permeability. VEGF also inhibits endothelial production of potent vasoconstrictor endothelin. VEGF physiological signalling VEGFR<sub>2</sub> maintains vascular tone by balancing NO and prostacyclin induced vasodilation and ET<sub>1</sub> regulated vasoconstriction. In connection with the foregoing, agents that block the VEGF pathway may lead to hypertension or BP destabilization. Functional and structural changes in the vascular area are likely mechanisms of hypertension development. Vasoconstriction is enhanced by a decrease in NO and prostacyclin production and an increase in endothelin production.<sup>9</sup>

Renal dysfunction is not the initial cause of hypertension in patients treated with VEGF inhibitors, but inhibition of renal NOS associated with impaired sodium excretion followed by fluid retention may contribute to the development of hypertension.<sup>7,8,10</sup> Blood pressure elevation is rapid in most patients; blood pressure should be monitored closely especially during the first 3-4 weeks after initial drug administration and resolves after withdrawal. In patients with advanced cancer, elevated BP was detected with sorafenib therapy on the first day of treatment and fully expressed at the time when balanced drug concentrations were reached around day

7.<sup>11</sup> Not only do patients face the risk of developing hypertension when starting treatment with VEGF pathway inhibitors but they are also at risk of developing hypotension upon withdrawal. Patients receiving therapy with VEGF-blocking drugs are often polymorbid and have an extensive cardiological history and medication. In all patients on a VEGF-blocking medication, newly introduced medication should be considered as a possible cause of hypertension in the differential diagnosis of sudden BP destabilization, the severity of the adverse side effect should be evaluated, and the relevant course of action should be followed accordingly.<sup>12</sup>

### GLUCOCORTICOIDS

The incidence of hypertension in patients with Cushing's syndrome is 70-80%, but only 15-20% in patients treated with high doses of synthetic corticosteroids that have lower mineralocorticoid activity than cortisol.<sup>13</sup> Oxidative stress and nitric oxide deficiency may be involved in the pathogenesis of glucocorticoid-induced hypertension.<sup>14</sup> However, the exact mechanism of glucocorticoid-induced hypertension is still not fully elucidated and appears to be multifactorial.

### IMMUNOSUPPRESSANTS

The incidence of hypertension in cyclosporine therapy is 50% and 35% for tacrolimus.<sup>5</sup> Everolimus and temsirolimus have antiproliferative effects which are used not only in transplantology to reduce lymphocyte proliferation, but also in oncology to influence tumor cell proliferation. The incidence of hypertension in both drugs has been reported in studies from 1 to 10%.<sup>15</sup> The mechanism of pressure elevation includes changes in the level of vascular endothelial function, decreased levels of vasodilatory mediators (prostacyclin and nitric oxide), increased levels of vasoconstrictive endothelin and increased insulin resistance.

### ERYTHROPOIETIN

Hypertension may develop in 20-30% of patients receiving erythropoietin, occurring 2 weeks to 4 months after initiation of treatment. The anticipated mechanism of this side effect is not exactly known, with increased calcium in vascular smooth muscle cells, activation of the local renin angiotensin aldosterone system, increased ET<sub>1</sub> production and reduced NO synthesis playing a certain role (2). Erythropoietin may increase BP by more than 10 mmHg, more often in patients on dialysis than in patients not yet on dialysis.<sup>2</sup>

## DRUGS AFFECTING THE EFFECT OF MINERALOCORTICOIDS

Drugs interfering with corticoid metabolism by influencing the activity of some important enzymes may contribute to hypertension. The antifungal agent posaconazole may lead to an excess of mineralocorticoids in the body by its mechanism of action.<sup>16</sup> Also, abiraterone, which is administered to patients with castration-resistant prostate cancer, leads to clinically significant corticoid imbalance in the body, cortisol deficiency, and an excess of mineralocorticoids.<sup>17</sup>

## NSAIDS

A meta-analysis conducted in the 1990s showed that non-steroidal anti-inflammatory drugs (NSAIDs) used more than 1 week in uncomplicated hypertensive and normotensive patients increased BP by an average of 5 mmHg.<sup>2</sup> The exact mechanism by which NSAIDs contribute to BP elevation is not fully understood and is multifactorial. NSAIDs inhibit cyclooxygenase 1 and 2, thus reducing prostaglandin synthesis, reducing NO and increasing ET1. NSAIDs reduce the efficacy of some antihypertensive drugs such as diuretics, betablockers and ACE inhibitors, but do not interfere with the action of calcium antagonists and centrally acting antihypertensive drugs.<sup>18</sup>

## SEX HORMONES

Hypertension is 2-3 times more common in women using oral contraceptives than in the control group.<sup>19</sup> Estrogens and progestins are believed to increase the synthesis of angiotensinogen in the liver, thereby increasing the production of angiotensin II and the secretion of aldosterone, which activates the mineralocorticoid receptor and causes sodium resorption and water retention. Testosterone causes increased sodium and water retention through androgen receptor agonism.<sup>2</sup>

## CONCLUSION

With exponential growth in pharmaceutical industry, several drugs which are generally perceived as a potential cause of hypertension development are now being used for prophylactic and therapeutic use across the globe. New salts that interfere with the pharmacodynamic effect of the body's regulatory mechanisms are already in the market and attention should be paid to this issue. Most patients with high blood pressure have essential hypertension or well-known forms of secondary hypertension such as renal parenchymal disease, renal artery stenosis,

hyperaldosteronism, or pheochromocytoma. Healthcare professionals are not too aware of drug associated increase in blood pressure. An accurate and detailed medical history detailing all medications being taken by the patient concomitantly or in past would help to identify the culprit drug in case of drug related hypertension. Identification of the intake of these substances may be important because their elimination can prevent the need for unnecessary, costly, and potentially dangerous evaluations, treatments, or both.

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# Hypercalcemia and Milk Alkali Syndrome: A Case Report

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A triad of metabolic alkalosis, hypercalcemia and renal insufficiency constitutes the milk alkali syndrome. Elderly subjects, especially those on drugs that GFR are more prone to acquire this syndrome. Those who take calcium supplements have high chances of developing milk alkali syndrome and this stands amongst the top five causes of hypercalcemia. Herein we present a case of hypercalcemia who was taking only small amount of calcium supplements but had a few concomitant risk factors.

**KEYWORDS:** Hypercalcemia, Milk Alkali Syndrome, Calcium

## INTRODUCTION

Milk-alkali syndrome is characterized by the triad of hypercalcemia, metabolic alkalosis and acute renal failure and is associated with the intake of large amounts of calcium and absorbable alkali.<sup>1,2</sup> Possible symptoms of hypercalcemia include debility and fatigue, muscle weakness, concentration disorders, nausea, vomiting, anorexia, constipation, polyuria, polydipsia, depressed mood, hypertension, arrhythmia and somnolence.<sup>3</sup> Aged females taking calcium carbonate supplements for osteoporosis or other reasons are too vulnerable to hypercalcemia. Milk alkali syndrome first was first identified in the beginning of 20<sup>th</sup> century. With the introduction of H<sub>2</sub> blockers and proton pump inhibitors, the incidence of Milk-alkali syndrome decreased, but a resurgence of this syndrome has been witnessed because of the wide availability and increasing use of calcium supplements.

## CASE REPORT

A 79-year-old female patient was referred by her family physician to evaluate her hypercalcemia. On admission, the patient complained of confusion, anorexia, nausea, polyuria, weakness in arms and legs, nausea and alternating stool consistency. Increasing forgetfulness in the past 2 weeks was reported by the accompanying person. Vital signs were in normal range, the patient was well oriented to place and time and no neurological deficits were noticed. Laboratory tests confirmed the presence of hypercalcemia at 2.8 mmol/L. Calcium levels at the family physician's clinic two days before were 3.5 mmol/L. The dose of the diuretic was increased in view of cardiac decompensation a few days before the

occurrence of hypercalcemia with a simultaneous increase in calcium supplementation. Other routine blood parameters were notable for increased creatinine at 158 pmol/L. The ECG, chest X-ray and urine examination were all normal. At the time of admission, patient was taking acetylsalicylic acid, lisinopril, furosemide, atorvastatin, calcium carbonate supplements and vitamin D. Parathyroid hormone levels were found to be low, excluding PTH-mediated hypercalcemia as well as primary hyperparathyroidism. Laboratory tests revealed reduced 1.25-OH-Vitamin D<sub>3</sub>.

Evidence of respiratory alkalosis was found on performing arterial blood gas analysis with a compensatory increase in carbon dioxide partial pressure. Further investigation revealed an increase in the bicarbonate levels. Calcium and vitamin D supplementation were stopped, diuretic therapy was discontinued and forced hydration was started for the treatment of hypercalcemia. Calcium levels the following day to 2.53 mmol/L and the patient reported a reduction in level of nausea, fatigue, weakness and polyuria. As calcium levels lowered down to normal and remained in range after forced hydration, malignancy or a paraneoplastic cause were excluded. Vitamin D intoxication was also ruled out as 25-hydroxy vitamin D<sub>3</sub> levels were in normal range. There was no evidence indicating pathological conditions like granulomatous diseases, sarcoidosis, tuberculosis or lymphomas. Hyperfunctioning thyroid and Adrenocortical insufficiency were also excluded on basis of normal TSH values (along with absent classic hyperthyroidism



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symptoms) and normal morning cortisol levels respectively. The congenital metabolic disorder of familial hypocalciuric hypercalcemia was ruled out on cross confirming the patient's previous checkup reports from family physician. High level of creatinine (167  $\mu\text{mol/L}$ ) and low glomerular filtration rate (24  $\text{mL/min/1.73 m}^2$ ) suggesting an acute renal failure noted in addition to hypercalcemia and metabolic alkalosis lead to a diagnosis of milk-alkali syndrome.

## DISCUSSION

Increased calcium levels are challenging for physicians and non-specific symptoms are problematic.<sup>3</sup> The search for a definite diagnosis is essential in view of the diverse treatment options. In hypercalcemic subjects, it is important to confirm the laboratory values with a second blood sample and correcting it against the serum albumin. This helps in ruling out pseudo-hypercalcemia occurring due to dehydration or other causes and helps in formulation of a correct diagnosis. Increased calcium is confirmed by a second blood sample and PTH determined simultaneously. Past medical history and records are also helpful in assessing the dynamics of the metabolic disorder. Majority of cases of hypercalcemia are due to primary hyperparathyroidism or a (para)neoplastic cause. A detailed drug history and evaluation of 25-OH-vitamin D<sub>3</sub> and 1,25-OH-vitamin D<sub>3</sub>, blood gas analysis, PTHrP and thyroid stimulating hormone are helpful in evaluating PTH-independent hypercalcemia.

Milk-alkali syndrome consists of hypercalcemia, various degrees of renal failure, and metabolic alkalosis due to ingestion of large amounts of calcium and absorbable alkali. This syndrome was first identified after medical treatment of peptic ulcer disease with milk and alkali was widely adopted during early 20th century [4]. Other differential diagnostic etiologies for hypercalcemia must also be excluded. When H<sub>2</sub> blockers and proton-pump inhibitors were introduced for medical use, there was a decrease in the incidence of milk-alkali syndrome. Milk alkali syndrome is reported to be the third most common cause of hypercalcemia after hyperparathyroidism and malignant neoplasms.<sup>5,6</sup> The commonly affected subjects have comorbid conditions or risk factors like elderly women taking calcium supplements for osteoporosis, subjects with chronic renal disease, people at high risk for volume depletion and people who use calcium supplements or antacids at high doses or drugs that may reduce the glomerular filtration rate.<sup>3</sup>

Hypercalcemia causes renal vasoconstriction with reduced GFR. The activation of calcium-sensing receptors in the ascending limb of the loop of Henle slows down sodium-potassium-chloride transporters, resulting in increased natriuresis and diuresis leading to a fluid deficit. Hypercalcemia also slows down ADH-dependent water reabsorption, which leads to further volume depletion and further reduces pre-renal glomerular filtration. Intake of absorbable alkalis, impaired renal function, and increased tubular bicarbonate absorption require and maintain metabolic alkalosis, which in turn leads to calcium reabsorption via a pH-sensitive calcium channel in the distal tubule, thereby maintaining hypercalcemia. Evidence based therapy consists of cessation of all calcium- and carbonate-containing or alkaline preparations and definite forced hydration at the start with calcium-free infusion solutions. Immediate administration of calciuric loop diuretics is not recommended since they may result in an electrolyte imbalance, hypovolemia or renal impairment.<sup>1</sup> The possible use of loop diuretics after rehydration should be assessed clinically based on volume status. Calcium-sparing diuretics are contraindicated. Bisphosphonates should not be used due to the high risk of consequent hypocalcemia with milk-alkali syndrome. Calcium levels returning to normal within a few days and remaining normal also indicates the presence of milk-alkali syndrome.

Evidence in the literature suggests that pure metabolic alkalosis may be absent in cases with pre-existing chronic renal failure.<sup>7</sup> It was suspected that suspending calcium carbonate intake and reducing diuretics in consultation with the family physician before referral interrupted the vicious circle of hypercalcemia, leading to reduction metabolic alkalosis and regression of hypercalcemia.

## CONCLUSION

The presence of non-specific symptoms such as nausea, fatigue, low threshold serum calcium and albumin-corrected calcium levels calculated should direct the healthcare professionals to take hypercalcemia into consideration. Detailed drug intake history and PTH measurement helps in formulating initial diagnosis of hypercalcemia. There are numerous causes of hypercalcemia like multiple myeloma, thyrotoxicosis, primary hyperparathyroidism, malignant neoplastic lesions and calcium or vitamin D intoxication. Milk-alkali syndrome should be considered if hypercalcemia, alkalosis and acute renal failure are present.

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# Assessment of Knowledge and Attitude towards Hepatitis B Infection among Health-Care Professionals in a North Indian City

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**INTRODUCTION:** Hepatitis B is an infection which occurs frequently worldwide. Hepatitis B virus is a DNA virus and is etiologically related to family Hepadnaviridae. Most of the cases of Hepatitis B virus infection do not have any symptoms when they are newly or chronically infected due to which there is silent spread of the infection which later causes serious liver disease. Incidence of the Hepatitis B virus infection among health-care professionals has been estimated to be 2–4 times more as compared to the general population.

**AIMS:** to assess the knowledge and attitude towards Hepatitis B infection among medical, dental, and nursing students in Bareilly city.

**MATERIALS AND METHOD:** A cross-sectional observational study was conducted among the medical and nursing students of Rohilkhand Medical College and Hospital and dental students of Institute of Dental Sciences, Bareilly through a self-reported questionnaire was distributed among all the students of the study who were present at the day. Statistical analysis used: p-value was calculated using Kruskal Walli's ANOVA test. A p-value of 0.05 or less was used as cut off level for statistical significance.

**RESULTS:** Total 222 students were selected out of which 60 were medical, 60 were dental and 102 were nursing. In our study medical students had better knowledge, attitude towards Hepatitis B infection than dental and nursing students.

**CONCLUSIONS:** None of the students of medical, dental, and nursing were fully aware on all aspects of Hepatitis B Virus infection and the vaccination status was found to be unsatisfactory which increased the risk to acquire Hepatitis B infection.

**KEYWORDS:** Knowledge, Hepatitis B, Health-care Professionals.

## INTRODUCTION

Hepatitis B is an infection which occurs frequently worldwide. Hepatitis B virus is a DNA virus and is etiologically related to family Hepadnaviridae.

Most of the cases of Hepatitis B virus infection do not have any symptoms when they are newly or chronically infected due to which there is silent spread of the infection which later causes serious liver disease. Every year about 10 lakh people die from this infection notwithstanding the fact that this infection could be prevented.

At present there are five identified viruses (hepatitis A, B, C, D and E) that specifically attack the liver to cause “viral hepatitis” or inflammation of the liver. Among all of the hepatitis viruses only the hepatitis B and C viruses result in “chronic” infection that may further lead to cirrhosis, liver cancer and liver failure.

Hepatitis B virus may remain inactive or cause significant liver disease (chronic carrier state) such as liver fibrosis, cirrhosis and finally terminal stage liver

disease.<sup>1</sup>

Hepatitis B virus is able to survive outside the human body for at least seven days but can still cause infection during this time period. The incubation period of the hepatitis B virus is 30 to 180 days and it can be detected within 30 to 60 days after infection.

Hepatitis B is most commonly spread through perinatal transmission i.e. from mother to child, or through horizontal transmission by exposure to infected blood. Chronic hepatitis B virus infection is very commonly seen in infants who have been infected from their mothers or infected otherwise.

The mode of spread can also be through exposure to infected blood and body fluids, such as saliva, semen and vaginal fluids and also by piercing, needlestick injury and tattooing.

Health-care workers are more knowledgeable than general population about the various infections and



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preventive measures to control them as they are being regularly trained.<sup>2</sup>

Incidence of the Hepatitis B virus infection among health-care professionals has been estimated to be 2-4 times more as compared to the general population.<sup>3</sup>

In hospital setup, Hepatitis B infection can be transmitted to medical, dental and nursing students through contact with blood or saliva of infected patients during treatment procedures, while drawing blood, giving injections, or suturing, and needlestick injuries sustained while performing the procedures. Hence from the view-point of occupational safety measures, all health-care workers should be vaccinated against Hepatitis B Virus.<sup>4</sup>

Hence, this study was conducted to assess the knowledge and attitude regarding HBV infection among health-care professionals in Bareilly city.

**MATERIALS AND METHOD**

A cross-sectional observational study was conducted among the medical and nursing students of Rohilkhand Medical College and Hospital and dental students of Institute of Dental Sciences, Bareilly.

Stratified random sampling method was done for selection of students. There were three natural groups – medical, dental and nursing students. The students were grouped by course as MBBS, BDS, and nursing then they were selected from each group by simple random method. The study subjects were made fully aware about the nature of the study and its design. Verbal informed consent was obtained and anonymity of the study participants was maintained throughout the study.

Total sample size taken was 222 out of which 60 were medical, 60 were dental and 102 were nursing students. A self-reported questionnaire was distributed among all the students of the study who were present at the day. The questionnaire was adapted from pre-tested and pre-validated questionnaires from previous studies.

The questionnaire included questions on various aspects of hepatitis B infection on knowledge and attitude towards hepatitis B infected patients.

The subjects were asked to mark one of the most appropriate answers for each question.

The data collected was entered in to the Microsoft Excel Sheet then the total number of responses was calculated and compared. p-value was calculated using Kruskal Walli’s ANOVA test.

A p-value of 0.05 or less was used as cut off level for statistical significance.

**RESULTS**

The present study was conducted among 222 participants out of which 162 were females and 60 were males. (Table 1) Mean age of the study population was 20.5 years.

MEDICAL		DENTAL		NURSING	
M	F	M	F	M	F
36	24	13	47	11	91

**Table 1.** Gender-Wise Distribution of the Study Subjects (M: Males, F: Females)

The knowledge and attitude responses of the medical, dental, and nursing students has been listed in in Table 2, 3, and 4.

*Knowledge on hepatitis B:* Results revealed that all the responders (100%) had heard of hepatitis B infection. When queried about the spread of hepatitis B, 23.3% of the medical students, 30% of the dental students, and 28.4% of the nursing students stated that hepatitis B was spread by blood transfusion, 36.7% of the medical students, 35% of the dental students, and 36.3% of the nursing students were of the opinion that it was spread by contaminated needles, 35% of the medical, 26.7% dental, and 26.5% nursing students concurred that it was spread by exposure to infected body fluids.

All of the participants (93.1%) believed that it was a viral infection except 6.9% of the nursing students who believed that it was a bacterial infection which was statistically significant.

86.7% of medical, 96.7% dental students believed that hepatitis B was life threatening but only 79.4% of the nursing students believed so which was statistically significant.

On whether they knew other types of hepatitis infections, 1.7% of medical, 5% of dental students were

		MEDICAL		DENTAL		NURSING		p value
Have you heard of hepatitis B?	Yes	60	(100%)	60	(100%)	102	(100%)	1.000
	No	0	(0%)	0	(0%)	0	(0%)	
Hepatitis B is spread by	Blood transfusion	14	(23.3%)	18	(30%)	29	(28.4%)	0.797
	Contaminated needles	22	(36.7%)	21	(35%)	37	(36.3%)	
	Exposure to infected body fluids	21	(35%)	16	(26.7%)	27	(26.5%)	
	Food prepared by infected persons	0	(0%)	0	(0%)	0	(0%)	
	Shaking hands with infected persons	0	(0%)	0	(0%)	0	(0%)	
	Use of infected razors	0	(0%)	0	(0%)	0	(0%)	
	Vertical transmission from mother to child	0	(0%)	1	(1.7%)	0	(0%)	
	Sexual intercourse	3	(5%)	4	(6.7%)	9	(8.8%)	
	Coughing	0	(0%)	0	(0%)	0	(0%)	
Hepatitis B is a _ infection?	Viral	60	(100%)	60	(100%)	95	(93.1%)	0.015*
	Bacterial	0	(0%)	0	(0%)	7	(6.9%)	
	Parasitic	0	(0%)	0	(0%)	0	(0%)	
Hepatitis B is life threatening?	Yes	52	(86.7%)	58	(96.7%)	81	(79.4%)	0.009*
	No	8	(13.3%)	2	(3.3%)	21	(20.6%)	
Have you heard of other types of hepatitis infections?	Yes	59	(98.3%)	57	(95%)	86	(84.3%)	0.005*
	No	1	(1.7%)	3	(5%)	16	(15.7%)	
Does hepatitis B infection lead to other types of hepatitis infections?	Yes	26	(43.3%)	43	(71.7%)	71	(69.6%)	0.001*
	No	34	(56.7%)	17	(28.3%)	31	(30.4%)	
How do you screen for hepatitis B infection?	HBsAg	59	(98.3%)	51	(85%)	47	(46.1%)	0.000*
	Anti-HBC	1	(1.7%)	6	(10%)	26	(25.5%)	
	Anti-HBE	0	(0%)	3	(5%)	29	(28.4%)	
Chronic hepatitis B infection can lead to	Cirrhosis	35	(58.3%)	26	(43.3%)	46	(45.1%)	0.165
	Carcinoma Liver	6	(10%)	7	(11.7%)	22	(21.6%)	
	Kidney disease	0	(0%)	0	(0%)	10	(9.8%)	
	Other liver disease	17	(28.3%)	20	(33.3%)	15	(14.7%)	
	Death	2	(3.3%)	7	(11.7%)	9	(8.8%)	

**Table 2.** Knowledge of Hepatitis B among the Study Population

unaware of other type of hepatitis infections whereas 15.7% of the nursing students were unaware regarding the same which was statistically significant.

98.3% medical and 85% dental students had correct knowledge regarding screening of hepatitis B infection but only 46.1% nursing students were aware of the same and again this difference was statistically significant.

Only 28.3% dental, and 30.4% of the nursing students were unaware of the fact that hepatitis B infection could lead to other types of hepatitis infection whereas more than half of the medical respondents (56.7%) were

unaware of the same. (p<0.001)

When asked about complications of chronic hepatitis B, 58.3% medical, 43.3% dental, and 45.1% of nursing students responded that chronic hepatitis B infection lead to cirrhosis and 10% of the medical, 11.7% dental, and 21.6% of the nursing students be vaccinated for hepatitis B. Only 91 % of the nursing students agreed that adults had to be vaccinated for hepatitis B which was statistically significant.

Most of the medical (75%) and dental (71.7%) students were completely vaccinated against hepatitis B while

		MEDICAL		DENTAL		NURSING		p value
Is Hepatitis B preventable?	Yes	55	(91.7%)	55	(91.7%)	69	(67.6%)	0.000*
	No	5	(8.3%)	5	(8.3%)	33	(32.4%)	
Are you aware of hepatitis B vaccine?	Yes	60	(100%)	60	(100%)	89	(87.3%)	0.000*
	No	0	(0%)	0	(0%)	13	(12.7%)	
Whether adults need to be vaccinated for hepatitis B?	Yes	60	(100%)	60	(100%)	91	(89.2%)	0.001*
	No	0	(0%)	0	(0%)	11	(10.8%)	
Whether children need to be vaccinated for hepatitis B?	Yes	59	(98.3%)	60	(100%)	97	(95.1%)	0.152
	No	1	(1.7%)	0	(0%)	5	(4.9%)	
Have you been immunized with hepatitis B vaccine?	Yes	45	(75%)	43	(71.7%)	47	(46.1%)	0.000*
	No	10	(16.7%)	10	(16.7%)	37	(36.3%)	
	Unsure	5	(8.3%)	7	(11.7%)	18	(17.6%)	

**Table 3.** Knowledge on Prevention of Hepatitis B among Study Population

only 46.1% of nursing students had done so which was again statistically significant.

*Attitude towards hepatitis B infected patients:* 73.3% medical, 66.7% dental and 68.6% of nursing students accepted that hepatitis B patients could be allowed to work routinely.

25% medical, 35% dental, and 13.7% of the nursing students believed that hepatitis B infected patients could perform strenuous exercise. (p=0.013)

75% medical, 68.3% dental, and 81.4% of the nursing students were of the view that hepatitis B infected patients should abandon sexual contact to prevent transmission of infection to their partners.

Around 25% medical and 45% dental students believed that medical personnel should refrain from treating patients infected with hepatitis B whilst only 12.8% of the nursing students opined so which was statistically significant.

Furthermore, 81.7% of medical, 72.5% of nursing, and 61.7% of dental students were of the view that medical students could be encouraged to take the vaccine through media awareness programs and the difference was found to be statistically significant.

**DISCUSSION**

Outcome of the Hepatitis B infection is dependent on the result of dynamic interaction between the virus,

host response and hepatocytes.<sup>6</sup>

Medical, dental, and nursing students are exposed to the occupational risk as they are the first line of contact between patients and medical care and hence are susceptible to infected patients and contaminated instruments. Naturally they are envisioned to perform activities related to preventive care in their formative years. It is imperative to bring the relative incidence of Hepatitis B infection down by proper education regarding its transmission and by immunization of all related health care personnel with the vaccine.

This study sought to evaluate the knowledge and attitudes towards hepatitis B infection among medical and nursing students of Rohilkhand Medical College and Hospital and dental students of Institute of Dental Sciences, Bareilly.

The results of the study showed good overall knowledge and attitude about hepatitis B infection among medical and dental students but was poor among nursing respondents. The reason for this may be due to the fact that since they were not required to diagnose Hepatitis B infection, much attention was not paid to this aspect. Still, it was an important aspect to prevent oneself from acquiring it.

When asked about knowledge of Hepatitis B infection like type of infection, whether it was preventable and whether they knew other types of Hepatitis infection, nursing students scored poorly when compared with



		MEDICAL		DENTAL		NURSING		p value
Whether hepatitis B patients can be allowed to work routinely?	Yes	44	(73.3%)	40	(66.7%)	70	(68.6%)	0.714
	No	16	(26.7%)	20	(33.3%)	32	(31.4%)	
Whether hepatitis B patients can be allowed to do strenuous exercise?	Yes	15	(25%)	21	(35%)	14	(13.7%)	0.013*
	No	45	(75%)	39	(65%)	88	(86.3%)	
Whether hepatitis B patients should abandon sexual contact?	Yes	45	(75%)	41	(68.3%)	83	(81.4%)	0.167
	No	15	(25%)	19	(31.7%)	19	(18.6%)	
Whether medical personnel should refrain from treating patients infected with hepatitis B?	Yes	15	(25%)	27	(45%)	13	(12.7%)	0.000*
	No	45	(75%)	33	(55%)	89	(87.3%)	
How can medical students be encouraged to take the vaccine?	Media awareness programs	49	(81.7%)	37	(61.7%)	74	(72.5%)	0.051*
	Others	11	(18.3%)	23	(38.3%)	28	(27.5%)	

**Table 4.** Attitude towards Hepatitis B Infected Patients; p<0.05: statistically significant, Kruskal Wallis ANOVA

dental and medical students.

When asked whether Hepatitis B was life threatening, and its complications, dental students had marginally better knowledge when compared to medical students which is in agreement with the study conducted by Tirounilacandin et al. where dental interns (34.7%) had better knowledge as compared to medical interns (32.8%).<sup>7</sup>

Majority of medical, dental and nursing students believed that Hepatitis B was spread by exposure to infected blood & body fluids which was similar to a study conducted in BJ Medical College, Gujarat that also showed a high level of knowledge (86.7%) regarding modes of transmission.<sup>8</sup> Contrarily, a study conducted by Paul P et al. in Tagore medical college and hospital, Chennai showed low level of knowledge regarding transmission.<sup>5</sup>

Majority of medical and dental students were aware about the screening for hepatitis B infection whereas only 46.1% of the nursing students had the awareness regarding the same which was statistically significant. This is in contrary to the study conducted by Paul P et al. where only 50.8% of the medical and dental students knew the correct answer.<sup>5</sup>

When asked about complications of Hepatitis B, the results showed very less knowledge among medical, dental, and nursing students which was in agreement to a study conducted by Paul P et al. in which very less respondents had correct knowledge.<sup>5</sup>

With regard to the vaccination status, higher proportion of medical students received vaccination as compared to dental and nursing students which was in contrast with the study conducted by Adenlewo et al. in Nigerian university where dental students (88.71%) received the vaccine more than medical students (76.47%) and the reason for not getting vaccinated was considered to be their busy schedule.<sup>9</sup>

In an Ethiopian study, 13.4% of the students received one or more doses of hepatitis B vaccine but only 4.7% of the students were fully vaccinated against Hepatitis B.<sup>10</sup>

The vaccination status in Muhammad medical college Mirpurkhas, was 87.8%,<sup>11</sup> 29.3% in medical students of BJ medical college,<sup>8</sup> 42% in medical students of Lahore.<sup>12</sup>

When asked whether hepatitis B patients can be allowed to work routinely and perform strenuous

exercise and whether medical personnel should refrain from treating Hepatitis B infected patients, nursing students scored better as compared to medical and dental students.

In our study medical students had better knowledge and attitude towards Hepatitis B infection than dental and nursing students.

Based on the results from this study, we can infer that there is a further need to improve knowledge about Hepatitis B Virus infection in medical, dental, and nursing students.

## CONCLUSION

This study concludes that none of the students of medical, dental, and nursing were fully aware on all aspects of HBV infection and the vaccination status was found to be unsatisfactory which increased the students' risk to acquire Hepatitis B infection. Hence, we need a regular continuing awareness program for all the students and it is recommended that schedule for Hepatitis B vaccination be made compulsory for all the students in the first year of their college.

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# Internet and its Impact on the Patient-Physician Relationship Patient Visiting Various Dental Clinics in Northern India

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**INTRODUCTION:** Readily available health-related information over the internet has led to increased patient awareness, and this might be a possible factor straining the patient-physician relationship.

**AIM:** To assess the impact of the internet on the patient-physician relationship amongst patient visiting various dental clinics in Northern India.

**MATERIALS AND METHODS:** Of the 600 pre-tested online questionnaires distributed, a total of 456 (response rate 76%) adequately filled questionnaires were analysed for the impact of internet on the patient-physician relationship. Responses were subsequently tabulated and analysed using SPSS Version 21.0. Statistical significance was kept as  $p \leq 0.05$ .

**RESULTS:** A statistically significant difference ( $p = .04$ ) was seen amongst males and females regarding their internet usage with a higher proportion of health information being sought by males. Most internet users (66.6%) followed their physician's advice before they began using the internet with behavioural changes seen mostly in the 18-30 years age group (75.64%), yet only 14.38% of them informing their physician about such changes.

**CONCLUSION:** It is important that people be advised about the potential risks of believing in sources from the internet with physicians also being advised to spend more quality time with their patients to alleviate them of their fears and doubts.

**KEYWORDS:** Internet, Information, Health

## INTRODUCTION

The generation of today is heavily dependent on the internet for information needs which has propelled India to second spot in terms of internet users after China and with 560 million active users. Furthermore, statistics reveal that nearly three fourths of India's online population is under 35 years of age.<sup>1</sup>

Before the advent of internet, patients relied heavily on their physicians for health based information and treatment modalities. But now, with easy access to information available on the web, patients are getting more knowledgeable regarding their health and at times, question the attending doctors about procedures and alternate options. In India, there were an estimated 72% of people who acknowledged the fact that they surfed the internet looking for health-related information out of which, a whopping 95% of the population found the information available on the internet serving their purpose.<sup>2</sup>

Searching for health-related information on the internet by patients has quite a few advantages for them. It helps them increase their knowledge,

competence, and engagement in health maintenance and decision-making, whilst also providing an opportunity to investigate difficult or embarrassing questions with comfort and privacy.<sup>3,5</sup> Patients also appreciate the freedom afforded by ready access to online health related sites, articles or resources, which reduces the time and commitment for office-based physician consultations. Also, the Internet provides space (anonymous, if required) to majority of patients who finding themselves in similar medical situations/conditions, and hence, helps in generating a strong, highly accessible base of care, as well as to understand and to provide support to individuals with similar issues related to their health.<sup>5</sup>

Hence, this study tries to assess the impact of internet on health related behaviours of patients and its impact on the physician-patient relationship amongst patients visiting various dental clinics in Northern India.

## MATERIAL AND METHODS

Data was collected from the questionnaire adopted by Iverson SA et al.<sup>6</sup> After adapting the questionnaire



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according to the Indian population, the questionnaire was Pre- tested it on 50 people for its content and criterion validity. After making minor adjustments, the Questionnaire was distributed online to as many patients visiting various dental clinics Northern India who gave a written consent to be a part of the study. Dentists having clinics in Northern India were contacted, asked to participate in the study and their patients were asked to fill the questionnaire through the Quick Response (QR) code of the clinic posted in their clinic. The patients' consent to participate in the study (inclusion criteria) was implied when they clicked on the "next" button to answer the questionnaire and they had complete freedom either to decline or answer the questionnaire. Access to data was only to the principal investigator and no personal details (e-mail id, phone number, name etc.) were asked. Responses were sought from only those patients who had had basic access to internet, were aged 18 and above, surfed the internet for at least 4 hours per week and could speak English fluently (inclusion criteria) and a submission was only considered when the "submit" button was clicked at the end of the questionnaire (inclusion criteria). Among total submissions, if a dentist failed to answer  $\geq 1$  question, it was excluded from the analysis. (Figure 1)

Data was analysed using SPSS version 21.0.<sup>7</sup> Descriptive statistics was applied and the Chi- square test was done to find out associations among different age groups.

## RESULTS

A total of 456 adequately filled questionnaires were identified from the 600 questionnaires distributed, leading to a response rate of 76%. The responses were subsequently tabulated and analyzed.

### *Demographic data of study population (Table 1)*

The study comprised of 51.3% males and 48.7% females respectively divided amongst different age groups. Most of the people (37.9%) visiting the college were 30-45 years of age. The majority of the population (73.2%) visited the dental college themselves as compared to just 17.69% of the people who accompanied someone for their treatment.

### *Responses of the various age groups to the questions asked in the survey (Table 2)*

There were a total of 400 (87.7%) internet users, majority (45.5%) of them belonged to 18-30 years age

group while the least (7.2) belonged to the age group of

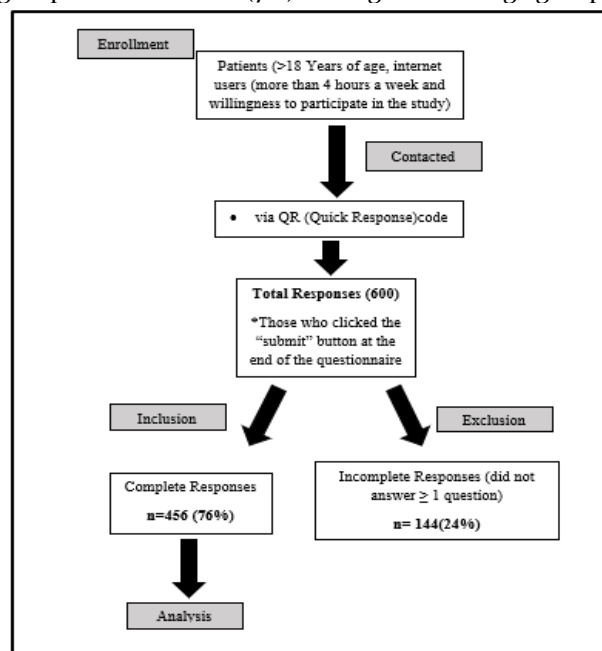


Figure 1. Study Protocol

$\geq 61$  years of age. Of the 12.3% of non internet users, most of them belonged to the age group of  $\geq 61$  years (42.9%). When enquired whether the internet users were able to find answers to their health related questions online, a total of 121 (30.3%) and 171 (42.8%) of the users replied "yes" and "somewhat" respectively, whereas 108 (26.9%) people were unable to find answers to their health related questions. A statistically significant difference was seen among all age groups who answered "yes" to a particular question ( $p=0.01$ ).

The third question, which selected information on whether respondents experienced changes in thinking about health as a result of online information, the age group of 18-30 years replied in the affirmative which was significant when compared to other age groups ( $p=0.03$ ).

Behavioral changes due to online information was seen most in the 18-30 years age group (30.0%), but only 15.9% of them informed their physician about such changes. The same trend was seen among the age group of 45-60 years where 41.1% of the respondents did not inform their physicians about such behavioral changes. No statistical significance was observed among the age groups, respectively. When it came to discussing online

Characteristic	AGE GROUP (n,%)				Total (n,%)
	18-30	30-45	45-60	≥60	
<b>Gender</b>					
• Male	12(41.4)	99(57.2)	54(42.2)	69(54.8)	234(51.3)
• Female	17(58.6)	74(42.8)	74(57.8)	57(45.2)	222(48.7)
<b>Total</b>	<b>29(6.4)</b>	<b>173(37.9)</b>	<b>128(28.1)</b>	<b>126(27.6)</b>	<b>456 (100)</b>
<b>Reason for visit</b>					
• For own treatment	16(55.2)	135(78)	99(77.3)	84(66.6)	334(73.2)
• Accompanying Someone	13(44.8)	38(22)	29(22.7)	42(33.4)	122(26.8)
<b>Total</b>	<b>29(6.4)</b>	<b>173(37.9)</b>	<b>128(28.1)</b>	<b>126(27.6)</b>	<b>456 (100)</b>

**Table 1.** Demographic data of the Study Population

health information, only the respondents between age groups of 46-60 years (41.1%) believed that their physician was willing to discuss online information with them. The difference in opinion among other age groups did not show any statistical significance.

Most internet users (10.6%) followed their physician's advice before they began using the internet. While only 9.8% followed their physician's advice "most of the time." No statistical significance was seen among the different age groups.

Amongst non-internet users (n =56) the main reason was that most of them did not trust internet information (30.6%).

## DISCUSSION

In an effort to assess the impact of internet on the patient- physician relationship, it was found that a total of 57.35% of the study population belonged to the "internet users" group who surfed the internet for most of their basic needs and out of these "internet users", a total of 67.4% of the population were able to find answers to their health questions online.

Males made up a slightly higher proportion compared to females seeking health information from the internet. This was in contradiction to various studies where a higher response rate was seen amongst women who sought more health related information when compared to males.<sup>6,8,9,10</sup>

This study found that internet usage decreased as age increases, and this was found to be in agreement to various studies.<sup>6,8,9,10,11,12</sup> It was also noted that although

a higher percentage of internet users were amongst the age group of 18-30 years, the possibility of their main use of the internet could be limited to socialising and entertainment, whereas older age groups specifically focus their internet usage on seeking health related information which was in agreement with this study.<sup>13</sup>

This study also revealed that only 30% of the respondents were willing to discuss online information with their physicians. This is in line with studies conducted by Ahmad FL et al. and Chestnutt IG et al. who also reported low willingness of patients to discuss information with their physicians.<sup>14,15</sup> Contrary to such results, Giveon et al. and Nili T et al. reported a positive attitude of respondents in discussing such information with their physicians<sup>16,17</sup>. It might be speculated that factors which can influenced patient- physician communication are the fear and anxiety levels of the patient, excessive work burden of the physician, the inherent fear of litigation by the patient, a possible fear of physical or verbal abuse coupled with unrealistic expectations lead the patient to seek help from easily available online health related information privately and securely.<sup>18</sup>

Majority of the non- internet users(56.2%) did not search the internet for health related information as thought that they were already adequately informed. This study also did not aim investigate their source of information which could range from reading medical magazines to believing in the hear-say of their peers and/or getting knowledge from people/ family members getting treatment for similar conditions. 1.5% of the population were "uncomfortable" with the internet, which could be due to inability to keep pace

QUESTIONS	AGE GROUP (IN YEARS)				
	18-30	31-45	46-60	≥61	Total
Internet users	182(45.5)	122(30.5)	67(16.8)	29(7.2)	400(100)
_ I am able to find answers to my health questions online					
-Yes	55(45.4)	26(21.5)	25(20.6)	15(12.5)	121(100)*
-Somewhat	82(47.9)	51(29.8)	29(16.9)	9(5.4)	171(100)
-No	45(41.6)	45(41.6)	13(12.0)	5(4.8)	108(100)
_ I have experienced changes in my thinking about health as a result of online information					
-Yes	103(39.2)	98(37.3)	43(16.3)	19(7.2)	263(100)
-No	79(57.6)	24(17.5)	24(17.5)	10(7.4)	137(100)
I made behavioural changes as a result of online information					
-Yes	45(30)	55(36.6)	39(26.0)	11(7.4)	150(100)*
-No	137(54.8)	67(26.8)	28(11.2)	18(7.2)	250(100)
I informed my physician about these behavioral changes					
-Yes	10(15.9)	39(61.9)	9(14.3)	5(7.9)	63(100)
-No	172(51.0)	83(24.6)	58(17.2)	24(7.2)	337(100)
I believe my physician is willing to discuss online information with me					
-Yes	22(25.3)	41(41.1)	15(17.2)	9(16.4)	87(100)
-No	160(51.1)	81(25.9)	52(16.6)	20(6.4)	313(100)
I followed physician's advice before I began using the Internet					
-Always	3(6.9)	12(27.9)	25(58.1)	11(7.1)	43(100)
-Most of the time	15(38.4)	10(25.6)	13(33.3)	2(2.7)	39(100)
-If advise made sense	20(41.6)	15(31.3)	11(22.9)	6(4.2)	48(100)
-Made up own mind	37(41.6)	31(34.8)	15(16.8)	7(6.8)	89(100)
-Seldom	107(59.1)	54(29.8)	3(1.7)	17(9.4)	181(100)
Non-internet users, N (%)	8 (14.3)	9 (16.1)	15(26.8)	24(42.8)	56 (12.3)
Reasons given for not using the Internet to locate information about health online					
-Already adequately informed	2(18.2)	1(9.1)	2(18.2)	6(54.5)	11(100)
-Use other resources	1(1)	2(20)	3(30)	4(40)	10(100)
-No internet access	2(28.6)	1(14.2)	2(28.6)	2(28.6)	7(100)
-Uncomfortable with internet	1(9.1)	2(18.2)	2(18.2)	6(54.5)	11(100)
-Do not trust internet information	2(11.8)	3(17.6)	6(35.3)	6(35.3)	17(100)
Total	8(14.3)	8(14.3)	15(28.5)	24(42.9)	56(100)

**Table 2.** Responses of The Various Age Groups to The Questions Asked in The Survey

with evolving technology and which could be solved in due course of time depending upon the individual's interest to learn. A minute percentage (5.4%) of the respondents did not trust the information on the internet.

Certain authors have stated that the availability of health information on the internet is generally beneficial for the patients<sup>19,20</sup>. This is in contradiction to certain authors who rationalise that the

interpretation of medical based information requires an acquired skill which patients often lack. The widespread availability of such information through the worldwide web, may fulfil the patients' search for knowledge, but they may fail to recognise that certain important information might be missing or they might fail to acknowledge the biased content of the information they obtain.<sup>21</sup> Failure to recognise non-evidence-based material by patients with a potential

for misinterpretation of some of the medical information might lead to serious health concerns.<sup>22</sup>

### LIMITATIONS

This study is prone to certain limitations which are:

1. The self-reported nature of data leads might have led to social desirability bias, recall bias or respondent bias.
2. It is possible that patients using the internet filled out the surveys more than those not using the internet.
3. Like this study, majority of the studies assessing the impact of internet on patient-physician relationship collected information at once (cross-sectional in nature). But mostly, physician-patient relationships are mostly long term which involve multiple visits, and this may limit the generalizability the results.<sup>23</sup>

### CONCLUSION

With the ever changing patterns of internet usage, it is important that patients be advised pertaining to the misleading nature of information present on the internet. It is equally important that physicians work towards elimination of barriers that might hamper an effective communication with their patients. With today's younger generation being short on time and having instant internet access on the go, it is important that they, in particular, be made aware of the potential harm any misleading information can create on their health and unnecessarily add to the global burden of disease.

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