# ARCHIVES OF THE TURKISH SOCIETY OF CARDIOLOGY

# Hypertension: A National Cross-Sectional Study in India

Hipertansiyon: Hindistan'da Ulusal Kesitsel Bir Çalışma

#### ABSTRACT

**Objective:** Hypertension is a global public health problem. This article aimed to estimate the national prevalence of hypertension in India for both women and men. The study had also examined the demographic and socioeconomic status of hypertensive women and men.

**Methods:** The study used the National Family Health Survey 4 from all over India. Hypertension of 661 771 women (15-49 years) and 104 357 men (15-54 years) and their demographic and socioeconomic variables were assessed. Crosstabulation, chi-square tests, and multivariate logistic regression were used.

**Results:** The prevalence of hypertension in women and men were 11.40% and 18.10%, respectively. State-wise, Sikkim had shown the maximum prevalence. Older women (45-49 years) and men (50-54 years) had the highest hypertension prevalence among all age groups. Urban people had shown proportionately more hypertension than rural people. Education, working status, and richer economic status emerged as significant risk factors. Women with lower educational status and men with higher educational status were more likely to be hypertensive. Working people were more hypertensive than their non-working peers. Economically, sound men were more hypertensive than poor people. Hypertensive people accessed medical care more.

**Conclusion:** There are various modifiable risk socioeconomic factors associated with hypertension. Policymakers can consider the current findings for better preventive planning. The risk factors identified in the study should be considered with appropriate weightage.

Keywords: Hypertension, India, healthcare, education, employment, economic status

#### ÖZET

**Amaç:** Hipertansiyon küresel bir halk sağlığı sorunudur. Bu makale, Hindistan'da hem kadınlar hem de erkeklerde ulusal hipertansiyon prevalansını tahmin etmeyi amaçladı. Çalışma ayrıca hipertansif kadın ve erkeklerin demografik ve sosyoekonomik durumunu da incelemiştir.

**Yöntemler:** Çalışma, Hindistan'ın her yerinden Ulusal Aile Sağlığı Araştırması 4'ü kullandı. 661 771 kadın (15 - 49 yaş) ve 104 357 erkek (15-54 yaş) bireyin hipertansiyonu ve bunların demografik ve sosyoekonomik değişkenleri değerlendirildi. Çapraz tablolama, ki-kare testleri ve çok değişkenli lojistik regresyon kullanıldı.

**Bulgular:** Kadınlarda ve erkeklerde hipertansiyon prevalansı sırasıyla %11,40 ve %18,10 idi. Eyalet bazında Sikkim maksimum prevalansa sahipti. Daha yaşlı kadınlar (45 - 49 yaş) ve erkekler (50 - 54 yaş) tüm yaş grupları arasında en yüksek hipertansiyon prevalansına sahiplerdi. Kentlerde yaşayanlar, kırsalda yaşayanlara göre orantılı olarak daha fazla hipertansiyon göstermişti. Eğitim, çalışma durumu ve daha zengin ekonomik statü önemli risk faktörleri olarak bulundu. Daha düşük eğitim düzeyine sahip kadınlar ve daha yüksek eğitim düzeyine sahip erkeklerin hipertansif olma olasılığı daha yüksekti. Çalışanların, çalışmayan akranlarına göre daha hipertansif oldukları belirlendi. Ekonomik olarak güçlü erkekler, yoksul olanlardan daha hipertansifti. Hipertansif insanlar tıbbi bakıma daha fazla erişmekteydi.

**Sonuç:** Hipertansiyon ile ilişkili çeşitli değiştirilebilir riskte sosyoekonomik faktörler vardır. Politika yapıcılar, daha etkili önleyici planlamalar için mevcut bulguları değerlendirebilirler. Çalışmada belirlenen risk faktörleri doğru şekilde değerlendirilmelidir.

Anahtar Kelimeler: Hipertansiyon, Hindistan, sağlık bakımı, eğitim, istihdam, ekonomik durum

ypertension or high blood pressure (BP) has a significant role in developing heart, brain, kidney, and other diseases and is a significant cause of premature death



**ORIGINAL ARTICLE** 

**KLÍNÍK CALISMA** 

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around the globe.<sup>1</sup> High BP directly does not cause symptoms.<sup>2</sup> Long-term hypertension is a significant risk factor for certain health problems such as coronary artery disease, stroke, heart failure, atrial diseases, chronic kidney disease, and dementia.<sup>3</sup>

Epidemiologically it was estimated that 1.13 billion people have hypertension worldwide.<sup>1</sup> According to a systemic review and meta-analysis, the prevalence of hypertension in highincome countries (LMICs) is more than in low-income countries. However, awareness, treatment, and control substantially are also more in high-income countries than LMIC.<sup>4</sup> As a result, now, two-third of hypertensive people lived in the LMICs.<sup>1</sup>

India is one of the LMICs. It is also a substantial public health problem in India.<sup>5,6</sup> Hypertension was responsible for 53.8%, 55.7%, and 54.3% deaths due to heart disease, stroke, and chronic kidney disease, respectively in India in 2016.<sup>7</sup> In 2010, the Government of India launched a program named National Programme for Prevention and Control of Cancer, Diabetes, Cardiovascular Diseases, and Stroke (NPCDCS) to prevent non-communicable disease-related deaths in India<sup>8</sup> to achieve the global target of reducing 25% hypertension-related premature deaths by 2025.<sup>1</sup>

The modern concept of causation of disease is multifactorial.<sup>9,10</sup> There are global disparities in the prevalence of hypertension, mainly due to the presence of multiple factors which are responsible for developing hypertension. Some of those factors are non-modifiable and some are modifiable.<sup>11-14</sup> We are more concerned about modifiable risk factors because they can be adjusted or changed to prevent the development of the disease. There are some modifiable risk factors of hypertension related to the socioeconomic status of the individuals.<sup>14</sup> By analyzing the socioeconomic characteristics of hypertensive patients, we can identify the vulnerable target groups to take preventive and promotive approaches of hypertension among them, which could in turn help to achieve the national and international health goals.

This article aimed to estimate the national prevalence of hypertension in India for both women and men. The study also examined the demographic and socioeconomic status of hypertensive women and men.

# Methods

The current study has used secondary data generated from the fourth National Family Health Survey (NFHS-4), conducted by the Government of India, in collaboration with Measures DHS.

# ABBREVIATIONS

ANM	Auxiliary Nurse Midwife
ASHA	Accredited Social Health Activist
BP	Blood pressure
CEB	Census enumeration blocks
IPV	Intimate partner violence
NFHS-4	Fourth National Family Health Survey
NPCDCS	National Programme for Prevention and Control of
	Cancer, Diabetes, Cardiovascular Diseases, and Stroke
PSUs	Primary sampling units

The NFHS-4 was conducted to generate consistent quality data on health and sociodemographic issues of both women of reproductive age (15-49 years) and men (15-54 years). The NFHS-4 used 3 stages of sampling techniques for the urban areas and 2 stages of sampling techniques for rural areas. Based on the 2011 population census sample frame, NFHS-4 used probability proportional to size to assign primary sampling units (PSUs) in the villages (for rural) and municipality wards (for urban). Then from each village, PSU households were randomly selected. In the urban areas, from each PSU, the census enumeration blocks (CEB) were randomly selected, and then from each CEB, households were randomly selected.

The fieldwork was conducted in 28 522 clusters in India, from January 2015 to December 2016 by a total of 789 trained field teams. Each field team had a field supervisor, 3 women and 1 man as interviewers, and 2 health investigators. Each team also had 1 driver. The field staff had received rigorous training for conducting household surveys, including biomarker tests.

Initially, NFHS-4 selected 601 509 household samples. From the selected households, a total of 699 686 women aged between 15 years and 49 years (97% of response rate) and a total of 112 122 men aged between 15 years and 54 years (92% of response rate) were interviewed. However, the NFHS-4 report has provided a detailed depiction of the survey procedure, sampling, technique, data collection, and handling.<sup>15</sup>

**Blood pressure measurement**: Following ethical guidelines and recommended rules, the study has included 661 771 women (15-49 years) and 104 357 men (15-54 years). BP was measured for each participant 3 times (with an interval of 5 minutes before reading) by an Omron Blood Pressure Monitor. As per the recommendation by the World Health Organization and by the Hypertension Society of India, any sample individual whose average systolic BP was >140 mm Hg or average diastolic BP was >90 mm Hg were considered to be hypertensive (high BP). The field staff have encouraged and recommended the hypertensive individual to visit a doctor for a full evaluation.<sup>15</sup> A more detailed information of data collection is described elsewhere.<sup>15</sup>

**Independent variables:** Age, place of residence, education, religion, economic status, health insurance coverage, health-care access, and working status were considered as independent variables.

For the women, there were 7 age groups (15-19 years, 20-24 years, 25-29 years, 30-34 years, 35-39 years, 40-44 years, and 45-49 years) while for men there was an extra age group (50-54 years). The residency had rural and urban categories. Education had 4 groups (no education, primary, secondary, and higher education). Religion had Hindu, Muslim, Christian, Sikhs, Buddhist, Jain, Jews, Parsi, and others. In the current analysis, the study had considered Hindu, Muslim, and other religion (non-Hindu or non-Muslim) where other religion was created consisting of Christian, Sikhs, Buddhist, Jain, Jews, Parsi, and others. The economic status was measured by the wealth index and categorized into 5 quintiles (richest, richer, middle, poorer, and poorest). Health insurance, accessed healthcare facility, and working status had binary options (yes or no).

Table 1. State-wise Hypertension Prevalence among Women and Men in India

	Women (%)	Men (%)
Andaman and Nicobar Islands	11.40	29.70
Andhra Pradesh	11.90	20.80
Arunachal Pradesh	20.20	28.30
Assam	20.10	28.10
Bihar	7.60	12.00
Chandigarh	10.30	17.80
Chhattisgarh	11.00	17.10
Dadra and Nagar Haveli	9.20	18.30
Daman and Diu	9.50	11.40
Delhi	8.70	11.40
Goa	10.00	18.20
Gujarat	11.90	17.20
Haryana	11.60	22.10
Himachal Pradesh	14.40	27.10
Jammu and Kashmir	13.40	17.80
Jharkhand	10.10	14.90
Karnataka	12.20	20.50
Kerala	9.00	13.40
Lakshadweep	14.00	15.30
Madhya Pradesh	10.10	14.40
Maharashtra	10.90	19.90
Manipur	13.70	25.00
Meghalaya	11.60	14.40
Mizoram	11.00	19.60
Nagaland	19.80	29.60
Odisha	11.00	15.40
Puducherry	11.80	22.20
Punjab	16.50	27.70
Rajasthan	8.60	15.10
Sikkim	20.40	34.10
Tamil Nadu	10.60	21.80
Telangana	12.00	19.20
Tripura	15.00	17.50
Uttar Pradesh	9.30	13.00
Uttarakhand	11.20	21.80
West Bengal	13.00	17.60

# Statistical Analysis

Chi-square tests were used to examine the differences in proportions of exposure to intimate partner violence (IPV) by demographic, socioeconomic, and empowerment variables. Multivariate logistic regression analysis was performed with all demographics, socioeconomic, and empowerment (including electronic) variables to assess their independent contribution in predicting exposure to IPV. Statistical Package for the Social Sciences (SPSS) v 25 (IBM Corp., Armonk, NY, USA) was used for the analysis. Statistical significance was considered at P < .05.

# Ethical Approval and Consent to Participate

The current study has used secondary data from NFHS-4 and needs no proper permission. However, the Institutional Ethical Review Board, IIPS, Mumbai, India, had examined and provided necessary ethical approval (ref. number/IRB/NFHS-4/01 1/2015) to NFHS-4.

# Results

In India, the prevalence of hypertension among women is 11.40% and among men is 18.10%. In the member states, Sikkim has the highest prevalence of hypertension for both women (20.40%) and men (34.1%). The lowest prevalence of hypertension was observed among women (7.6%) in Bihar and men in Delhi, Dadra, and Nagar Haveli (11.4%). Table 1 presents the state-wise hypertension prevalence among women and men in India.

Figure 1 demonstrates the prevalence of hypertension in India among women and men by their age groups. The figure demonstrates that the prevalence of hypertension increases as age increases.

Table 2 indicates that the oldest women (45-49 years) and men of the oldest age groups have the highest prevalence of (26.3% and 33.1%, respectively) of hypertension in India. Females (12.2%) and males (20.3%) from urban areas were proportionally more hypertensive than rural areas. Females with no educational status (14.9%) and males with higher educational status (20.4%) were proportionally more hypertensive than their peers. Both women (14.6%) and men (23.3%) who believe in religions other than Hindu or Muslim were more hypertensive. Both the richest women (12.6%) and the richest men (22.6%) had the highest hypertensive prevalence. Similarly, both women (12.5%) and men (20.4%) having health insurance coverage were proportionally more hypertensive than those who had no coverage. Women (12.4%) and men (18.5%) who accessed the healthcare facility were proportionally more hypertensive. Working women (12.2%) and men (20.6%) were proportionally more hypertensive than non-working people.

Table 3 indicates that younger women and men were less likely to be hypertensive. Women with the primary educational status (adjusted (adj.) odds ratio (OR): 1.160; CI: 1.063-1.266) were more likely to be hypertensive in comparison to women with higher educational status. However, men with no education (adj. OR: 0.85; CI: 0.795-0.909), primary education (adj. OR: 0.909; CI: 0.852-0.97), and secondary education (adj. OR: 0.933; CI: 0.889-0.979) were less likely to be hypertensive than the men with higher education. Muslims were less likely to have hypertension than Hindus. Non-Muslim and non-Hindu men were more likely (adj. OR: 1.347; CI: 1.283-1.414) to be hypertensive than Hindu men. Poorest women were less likely (adj. OR: 0.884; CI: 0.817-0.956) and richer women were more likely (adj. OR: 1.076; CI: 1.013-1.143) to

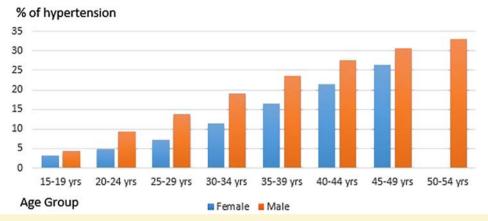


Figure 1. Prevalence of hypertension among women and men by their age groups. Women of reproductive age (15 -49 years). Men 15 -54 years.

be hypertensive than the richest women. Poorer men were less likely to have hypertension than the richest men. Non-working

women were more likely (adj. OR: 1.070; CI: 1.023-1.119) to be hypertensive than working women.

Sociodemographic variables	Ν	N Female Hypertensive (%) N		Male Hypertensive (%)	
Age group		P < .001		P < .001	
15 - 19 years	3699	117 264 (3.2)	796	17 686 (4.5)	
20 -24 years	5561	116 287 (4.8)	1434	15 473 (9.3)	
25-29 years	7937	108 861 (7.3)	2065	14 970 (13.8)	
30-34 years	10 583	91 954 (11.5)	2602	13 629 (19.1)	
35-39 years	14 067	85 717 (16.4)	3044	12 956 (23.5)	
40-44 years	15 625	72 699 (21.5)	3075	11 183 (27.5)	
45-49 years	18 140	68 989 (26.3)	3200	10 440 (30.7)	
50-54 years			2653	8020 (33.1)	
Residence		P < .001		P < .001	
Rural	52 263	469 658 (11.1)	12222	71 650 (17.1)	
Urban	23 349	192 113 (12.2)	6647	32 707 (20.3)	
Education		P < .001		P < .001	
No education	27 985	187 517 (14.9)	2742	14 001 (19.6)	
Primary	11 338	84 094 (13.5)	2644	13 456 (19.6)	
Secondary	30 117	315 498 (9.5)	10188	60 732 (16.8)	
Higher	6172	74 662 (8.3)	3295	16 168 (20.4)	
Religion		P < .001		P < .001	
Hindu	53 133	494 063 (10.8)	13892	78 455 (17.7)	
Muslim	11 122	89 714 (12.4)	2260	14 236 (15.9)	
Others	11 357	77 994 (14.6)	2717	11 666 (23.3)	
Economic status		P < .001		P < .001	
Poorest	12 955	126 853 (10.2)	2377	17 338 (13.7)	
Poorer	15 310	141 600 (10.8)	3300	21 730 (15.2)	
Middle	15 582	139 001 (11.2)	4019	22 647 (17.7)	
Richer	16 210	130 849 (12.4)	4413	21 543 (20.5)	
Richest	15 555	123 468 (12.6)	4760	21 099 (22.6)	

		Female			Male	
	Odds Ratio (ORs)	CI Lower Limit	Cl Upper Limit	Odds Ratio (ORs)	Cl Lower Limit	Cl Upper Limit
Age group						
15-19 years	0.087	0.079	0.095ª	0.098	0.089	0.107ª
20-24 years	0.132	0.122	0.144ª	0.204	0.189	0.219ª
25-29 years	0.203	0.189	0.219ª	0.316	0.295	0.338ª
30-34 years	0.341	0.319	0.364ª	0.472	0.442	0.503ª
35-39 years	0.547	0.514	0.581ª	0.621	0.583	0.661ª
40-44 years	0.772	0.727	0.819ª	0.767	0.72	0.817ª
45-49 years	Ref.			0.902	0.847	0.961⁵
50-54 years				Ref.		
Residence						
Rural	Ref.			Ref.		
Urban	1.030	0.983	1.080	1.042	1.002	1.084 <sup>b</sup>
Education						
No education	1.068	0.983	1.161	0.85	0.795	0.909ª
Primary	1.160	1.063	1.266 <sup>b</sup>	0.909	0.852	0.97 <sup>b</sup>
Secondary	1.099	1.021	1.182	0.933	0.889	0.979 <sup>⊾</sup>
Higher	Ref.			Ref.		
Religion						
Hindu	Ref.			Ref.		
Muslim	0.728	0.688	0.770ª	0.912	0.867	0.96ª
Others	0.981	0.913	1.054	1.347	1.283	1.414ª
Economic status						
Poorest	0.884	0.817	0.956 <sup>b</sup>	0.61	0.57	0.652ª
Poorer	0.935	0.871	1.004	0.69	0.65	0.731ª
Middle	0.980	0.917	1.046	0.818	0.776	0.864ª
<sup>a</sup> P < .001, <sup>b</sup> P < .05						

#### Table 3. Multivariate Logistic Regression Predicting Hypertension by Demographics and Socioeconomic Factors

# Discussion

In India, the prevalence of hypertension among women is 11.40% and among men is 18.10%. A systematic analysis using data from 70 countries indicated that the prevalence of hypertension globally for women is 30.1% and for men is 31.9%.<sup>4</sup> In high-income countries, the prevalence among women was 25.3% and among men was 31.6%, and in low- and middleincome countries, the prevalence among women was 31.2% and among men was 31.7%.<sup>4</sup> The prevalence of hypertension in Bangladesh was 20%,<sup>16</sup> Sri Lanka was 23.7% (male 23.4%, female 23.8%),<sup>17</sup> Pakistan was 8%,<sup>18</sup> Nepal was 28.4%,<sup>19</sup> and Bhutan was 17.4%.<sup>20</sup> The current study in India shows the lowest hypertension prevalence among 20-24 years: women 4.8%, men 9.3%, and among 25-29 years: female 7.3%, men 13.8%. We have also found that hypertension prevalence among age group 30-34 years: female 11.5%, male 19.1%, among 35 -39 years: women 16.4%, men 23.5%; among 40 -44 years: women 21.5% and men27.5% and among 45-49 age group: women 26.3% and men 30.7%.

Sikkim showed the highest prevalence of hypertension in India. The probable reason could be the dietary pattern in Sikkim including local traditional alcohol (known as Chang), which leads to metabolic syndromes and diabetes, and eventually, hypertension. A previous study indicated that the women in Sikkim have a relatively larger waist circumference.<sup>21</sup> Delhi has the lowest prevalence of hypertension for both genders. A further investigative study is warranted to explore the cause, especially whether ethnicity is playing a role or not. Sikkimese hypertensive patients are mostly from Sikkim. Delhi is the capital city and a cosmopolitan area where people from all over India reside. Dietary pattern, physical exercise, work stress, job role, ethnicity, family structure, tobacco use, alcohol consumption and other evidence-based risk, and protective factors could be explored behind such statewise differences of hypertension prevalence in India.

The study results indicate that people of lower age groups are less likely to be hypertensive than upper age groups. It is a biological phenomenon because age is one of the non-modifiable risk factors of hypertension.<sup>14,22</sup> Higher the age higher the prevalence of hypertension.<sup>23</sup> Therefore the Indian scenario of hypertension and age is at par with the international scenario, as indicated by a recent systematic review and meta-analysis.<sup>24</sup> Urban people and the working-class had proportionately more hypertension than rural people and non-working groups also. Previous studies support the current findings.<sup>6,25</sup> Stressful lifestyle in urban areas and work-related stress could be responsible for the higher prevalence. Stress is an important factor for hypertension. The human body liberates surge hormones in stress which temporarily causes a faster heartbeat leading to hypertension.<sup>26</sup> In urban areas, awareness and BP measurement is not up to the level, mainly due to lack of healthcare access. On the other hand, in rural areas in India community-level health workers such as Accredited Social Health Activist (ASHA) and Auxiliary Nurse Midwife (ANM) measures BP during home visits. Rural Indians may get a better opportunity than their urban peers. ASHA or ANM visits households and may measure BP and advice for consulting medical practitioners. Therefore, the rural people may get a better awareness of hypertension and get the opportunity for antihypertensive medication, if necessary. However, in densely populated urban areas, there is no opportunity to visit households and to measure BP. As a result, urban people do not know whether s/he has BP or not and hence do not receive any necessary medicine. Also, rural people have more physical activities than urban people.

People from other religions are proportionately more hypertensive than Hindus. Muslims are less likely to have hypertension than Hindus. For exploring the right reasons, the current study demands further clinical and non-clinical public health explorative studies. This study revealed that educational status is an important determinant of hypertension in India. Educated people are more conscious about their health, leading to their better access to healthcare. The current study has found that persons accessing the healthcare facility are proportionally more hypertensive. It could be that the persons are already aware of their hypertension and hence accessing healthcare. However, indepth future studies can better explain the reasons.

Compared to a higher educated woman, other women were more likely to be hypertensive and other men were less likely to be hypertensive. In the Indian context, we can relate the finding with woman empowerment. Educational status is one of the important indicators of woman empowerment. Less the educational status less the empowerment leads to more stress and domestic violence. An educated woman can make the economic decision of the family.<sup>27</sup> There are some studies that show the inverse relationship of education with the prevalence of coronary heart disease with hypertension.<sup>28-34</sup> Studies conducted in rural India showed higher consumption of tobacco in patients with lower educational status.<sup>35,36</sup> Tobacco is a risk factor for the development of hypertension. In the case of men, those who are higher educated are economically more empowered and more stressed. Income has a relation with educational status.<sup>37</sup> Long continued stress is one of the associated circumstances for economically empowered persons. Higher educational level which is associated with more stress and reduced sleep duration leads to development of hypertension. Increased stress in economically sound patients addicted to consuming energy drinks poses another risk for hypertension.<sup>38</sup> Higher income is associated with higher prevalence of hypertension.<sup>28-34</sup> Increased income leads to more exposure of hypertension risk factors including alcohol consumption, smoking, tobacco intakes, lack of physical activities with a sedentary lifestyle, stress, incensement of risk-taking behavior,<sup>39-41</sup> affecting mainly the men in India. In India, most families are economically dependent on men. In the majority of the families, they are the bread earners.<sup>42-44</sup>

In the case of women and men with health insurance coverage, proportionately hypertension is higher. In general, unhealthy people purchased health insurance to save her/his life in case of emergencies and for greater healthcare access. Indian context of hypertension shows both the awareness for acute health-seeking, as well the comparative wealthier people with several risk factors are prone to hypertension.<sup>45-49</sup>

# Limitations

The current study is a cross-sectional study. Therefore, the causality assigned in the study should be validated through longitudinal studies. One of the limitations of the current study is that it was conducted among women aged between 15 years and 49 years and among men aged between 15 years and 54 years. The study does not represent the elderly Indians and focuses mainly on young and middle-aged individuals. A further research study should be conducted including the older age group to explore the unrevealed fact. The survey has maintained the utmost quality control and time-verified methods. However, many issues raised in the study should get better answers through qualitative studies.

### Conclusion

There are various modifiable socioeconomic risk factors associated with hypertension. Policymakers can consider the current findings for better preventive planning. The risk factors identified in the study should be considered with appropriate weightage.

**Data Availability Statement:** Data is available from the NFHS-4 study from International Institute for Populations Sciences, Mumbai, India.

**Ethics Committee Approval:** The current study has used secondary data from NFHS-4 and needs no proper permission. However, the Institutional Ethical Review Board, IIPS, Mumbai, India, had examined and provided necessary ethical approval (ref. number/IRB/NFHS-4/01\_1/2015) to NFHS-4.

Informed Consent: The current study has used secondary data.

Peer-review: Externally peer-reviewed.

**Author Contributions:** Concept – K.D.; Design – K.D.; Supervision – K.D.; Literature Search – S.C., G.U., M.S.L.; Writing – S.C., G.U., M.S.L., K.D.; Critical Revision – M.S.L., K.D.

**Declaration of Interests:** The authors declare that they have no competing interest.

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