Risk Factors of Pregnancy-Induced Hypertension in Block Hazratbal of District Srinagar, Jammu & Kashmir----a Prospective Longitudinal Study

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ABSTRACT

INTRODUCTION: The term Pregnancy induced hypertension (PIH) refers to a disorder of blood pressure that arises because of the state of pregnancy. PIH is defined as new onset hypertension with or without significant proteinuria emerging after 20 weeks of gestation, during labour, or in first 48 hours post-partum. Objectives: To find out the risk factors of PIH in block Hazratbal, Srinagar. METHODOLOGY: A Community based longitudinal study was conducted in Block Hazratbal (District Srinagar) for a period of 18 months. All the pregnant females attending the antenatal clinic at the subcenters and PHCs were included in the study and assessed for eligibility. The pregnant women enrolled in the study were examined again around 30 weeks, 37 weeks and once in postnatal period. The information was collected from the study subjects on the basis of pretested semi-structured questionnaire regarding age, educational status, income per capita, occupation, family history of PIH, history of (H/O) hypertension in any family member, H/O addiction, physical activity, gravidity, parity, time since last child birth, H/O PIH in previous pregnancy, height, weight, anemia, edema, gestational age at delivery, fetal gender mode of delivery. RESULTS: Incidence of PIH increased with increasing age and was much higher among those study subjects who had a history of PIH in the previous pregnancy, who had a family H/O PIH, who delivered twins, who had a H/O hypertension in any family member, who had edema at baseline examination and who delivered male babies. DISCUSSION AND CONCLUSION: Risk factors of PIH include increasing age, H/O PIH in past, family H/O PIH, family H/O hypertension, male gender of fetus, twin pregnancy and edema in early pregnancy. PIH is a major cause of perinatal mortality, preterm delivery, IUGR, and maternal morbidity and mortality. Awareness about PIH and its risk factors among females and health care workers must be generated.

Keywords: PIH, Risk factors, Twin pregnancy, Srinagar.

How to cite this article: Rouf Hussain Rather, Umar Nazir, Shazia Benazir, S Mohammad Salim Khan. Risk Factors of Pregnancy-Induced Hypertension in Block Hazratbal of District Srinagar, Jammu & Kashmir----a Prospective Longitudinal Study. International Research Journal of Public Health, 2019; 3:27

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INTRODUCTION
Pregnancy is a physiological state which a woman experiences at some point of her life. During pregnancy a woman may develop complications which pose a risk to both maternal and fetal health. United Nations estimates of Maternal mortality showed that number of maternal deaths globally in year 2000 was 529,000, 99% of which were in developing countries with India contributing 136,000 maternal deaths\(^1\). The maternal deaths can be due to direct and indirect causes, of which direct causes like haemorrhage, infections, preeclampsia and eclampsia, obstructed labour and abortions contribute to 80% of total maternal deaths. Among these complications, hypertension during pregnancy contributes significantly (12%) to the maternal mortality\(^2\). The association of hypertension with proteinuria during pregnancy markedly increases the risk of perinatal mortality and morbidity\(^3\).

PIH is defined as hypertension (blood pressure $\geq 140/90$ mmHg) with or without proteinuria (≥ 300 mg/24 hours) emerging after 20 weeks of gestation, but resolving up to 12 weeks postpartum, in a previously normotensive, normoproteinuric woman. It is classified as gestational hypertension (without proteinuria), preeclampsia (with proteinuria), and eclampsia (associated with convulsions).

PIH along with haemorrhage & infection, contribute greatly to maternal morbidity & mortality\(^1\). World Health Organization estimates that at least one woman dies every seven minutes from complications of hypertensive disorders of pregnancy. Pregnancies complicated with hypertensive disorders are associated with increased risk of adverse fetal, neonatal & maternal outcome including preterm birth, intrauterine growth retardation (IUGR), perinatal death, antepartum haemorrhage, postpartum haemorrhage & maternal death\(^4\). Most deaths in PIH occur due to its complications & not due to hypertension per se.

The hypertensive disorders of pregnancy are a leading cause of maternal and perinatal mortality and morbidity in India and internationally. The management of PIH is aimed at termination of pregnancy, but this cannot be done in all cases, as most cases are preterm or very preterm. The pregnancy can be prolonged by using antihypertensive agents till a period where in foetal survival is good ,thereby maximizing the gestational age of infant and minimizing the foetal exposure to medication that may have adverse effects. The antihypertensive agents have a role in controlling hypertension and thereby maternal and foetal complications can be avoided\(^5,6,7\).

RATIONALE OF THE STUDY
PIH is one of the most common disorders seen in human pregnancies. Though relatively benign on its own, in roughly half of the cases the disorder progresses into pre-eclampsia, a dangerous condition that can prove fatal to expectant mothers. Also the fetus is at increased risk for a variety of life-threatening conditions.

Although various hospital based studies have been done in different parts of the country to describe the risk factors of PIH but no such community-based study has been conducted in Kashmir, so this study will be an endeavour to know the risk factors of PIH ; so that appropriate measures are being taken to prevent its occurrence and progression and improve the outcome of such cases.

Aims and Objectives
To find out the risk factors of pregnancy-induced hypertension in block Hazratbal, district Srinagar.

MATERIALS AND METHODOLOGY

Study Design: Community based longitudinal study.

Study Period: The study was done for a period of 18 months from April 2015 upto September 2016. During the first 12 months data was collected and during the next 6 months data entry, analysis and write-up was carried out.
Study Area: Study was conducted in the field practice area of GMC Srinagar which is Block Hazratbal (District Srinagar). Hazratbal block is a semi urban area of srinagar situated 12 kilometers from the centre of city and is under the administrative control of Department of Community Medicine, Government Medical College Srinagar. It comprises of 65 villages/wards which have been divided into four zones viz; Hazratbal, Harwan, Nishat, and Tailbal and the total population of the area is about 75083 (As per Block survey report BMO Hazratbal APRIL 2013). The block has four primary Health centres and 12 sub centers.

Sample size estimation
As per the table of estimating the sample size of a study for calculating the incidence rate with a specified relative precision from the manual SAMPLE SIZE DETERMINATION IN HEALTH STUDIES By S. K. Lwanga and S. Lemeshow, World Health Organization Geneva 1991, using the formula:

\[ n = \left( \frac{z_{1-\alpha/2}}{\varepsilon} \right)^2 \]

Where \( n \) is the sample size, \( z \) is 1.96, \( \alpha \) is type 1 error, and \( \varepsilon \) is relative precision. In this study, keeping relative precision at 10% and confidence level at 95%, the sample size came out to be 385.

Selection of sample and data collection:
All the pregnant females attending the antenatal clinic at the subcenters and PHCs during the data collection period were included in the study and assessed for eligibility, till the desired number of 385 eligible pregnant females was reached. The information was collected from the study subjects on the basis of pretested semi-structured questionnaire. The information was collected regarding age, literacy, residence, income, parity, history of PIH in the previous pregnancy, family history of hypertension or PIH, outcome of previous pregnancy etc. Prior to the enrolment of pregnant women, they were apprised of the purpose of the study and then their consent was sought.

Inclusion Criteria
- All normotensive pregnant women less than 20 weeks of gestation.

Exclusion Criteria
- Any Pregnant woman if found hypertensive before 20weeks of gestation.
- Any pregnant woman if found to be already on any prescribed antihypertensive medicine.
- Any pregnant if found to be more than 20 weeks of gestation at baseline examination.

All pregnant women less than 20 weeks of gestation were checked for blood pressure three times in the right upper arm and the lowest reading of the three was taken. The blood pressure of these pregnant women was checked at least once between 16th and 20th week of pregnancy. The pregnant women whose blood pressure was never equal to or more than 140/90 mmHg during their check-ups were included in the study. Also information was collected from the included pregnant women regarding their socio-demographic profile based on a semi-structured questionnaire. For better coverage, the zonal headquarters and their sub-centres were visited on the respective antenatal days. The pregnant women enrolled in the study were examined again around 30 weeks, 37 weeks and once in postnatal period and blood pressure was measured every time using the same procedure.

Operational definitions of Variables Used In The Study
Hypertension: For recording Blood Pressure, the woman was made to sit comfortably on a stool after 15 minutes of rest in the waiting area. The blood pressure was recorded in the sitting position by the standardized sphygmomanometer with appropriate cuff size. A rise in the blood pressure to the extent of 140/90 mmHg or more was labelled as Hypertension.
Proteinuria: All the women whose blood pressure was 140/90mmHg or above at any of the three follow-ups were subjected to Urine Examination for the presence of proteins in the urine by Uri-stick Test. Presence of protein ≥ 0.3gm/l in a clean- catch, mid-stream specimen of urine was labelled as Proteinuria.

PIH: Any woman who developed hypertension on any of the follow-ups was labeled as PIH. If hypertension was associated with Proteinuria it was labeled as a case of Preeclampsia and if without Proteinuria then it was labeled as a case of Gestational Hypertension. Any pregnant woman with Preeclampsia was referred to PHC Hazratbal for further investigations and management. Any woman suffering from Pregnancy-induced Hypertension if developed convulsions during antenatal, intranatal or post-natal period was planned to be labeled as a case of Eclampsia and to be immediately referred to nearby First Referral Unit.

Age: Age was recorded as on last birthday in years as per the records or statements of the individual. Marriage-age and the age of older child was ascertained to reach the nearest age, in case, the woman was not sure of her age.

Pregnant woman: Woman in the reproductive age group having history suggestive of physiological amenorrhoea which is the most common presentation of pregnancy, was confirmed by laboratory test, USG and physical examination.

Gravidity: Denotes the pregnant states both present and past irrespective of period of gestation.

Parity: Denotes the previous pregnancy beyond the period of Viability.

Physical Activity: Based on the recommendations of WHO expert Committee.

1. Sedantary: Viz. Office workers, Most Professionals (doctors, Lawyers, accountants, teachers, architects etc.) Shopkeepers, housewives with mechanical household appliances or with maids.

   2. Moderate: Viz. Students, farm workers, building workers (excluding heavy labourers), housewives (home-makers) without mechanical household appliances and without maids.


Occupation:
1. Labourer: Skilled: Carpenters/Masons etc.
   Unskilled: Labourers/Farmers etc.

2. Service: Professionals: Doctors/Engineers etc.
   Non – professionals: clerks/teachers etc.

   Petty: Shopkeepers/Rehriwallas.

4. Others: Housewife/home maker

Literacy: Literacy level was obtained as illiterate, just literate, primary, middle, high school, higher secondary, graduate, post-graduate and professional Level. Just literate included those people who did not have formal education but still can read and write slightly. Formal education is obtained in school.

Blood Pressure: It was recorded by standardized Mercury Sphygmanometer to label the woman normotensive or hypertensive.

Statistical analysis
The data was entered in the Microsoft excel and analysed using SPSS v16. Chi square test was used to see the association between two categorical variables. Wherever chi square was not feasible, Fisher’s exact test was used. To compare continuous variables between two groups T test was used.

OBSERVATIONS AND RESULTS
The study was conducted in 385 pregnant women with a mean age of 31.06 ± 4.537 years. Majority of the study subjects were 21 – 30 years of age (55.6%), home makers (96%),
doing moderate physical activity (95%) and multigravida (62.3%). Around one-fifth (19.1%) of the study subjects with para ≥ 1 had a history of PIH in the previous pregnancy and 7.5% of the study subjects had a history of PIH in mother or sister. More than half (52.5%) of the study subjects had a family history of hypertension. About two-fifths (39.7%) of the study subjects had pallor and 11.7% had edema at the baseline examination. Less than 2% of the study subjects delivered twins. Out of 391 children born, 2 were born dead and 55.2% were of male gender.

Incidence of PIH increased with increasing age among study population. It was much higher among those study subjects who had a history of PIH in the previous pregnancy, who had a family H/O PIH and who delivered twins. Incidence of PIH was also higher among those study subjects who had a H/O hypertension in any family member, who had edema at baseline examination and who delivered male babies.

Table 1: Distribution of different categorical variables among study subjects.

<table>
<thead>
<tr>
<th>Variable</th>
<th>≤ 20</th>
<th>21-25</th>
<th>26-30</th>
<th>31-35</th>
<th>36-40</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>2.6%</td>
<td>15.1%</td>
<td>40.5%</td>
<td>30.6%</td>
<td>11.2%</td>
<td>100.0%</td>
</tr>
<tr>
<td>Education status</td>
<td>Illiterate</td>
<td>Just Literate &amp; Primary</td>
<td>Middle</td>
<td>High School</td>
<td>Higher Secondary</td>
<td>Graduation &amp; Post-graduation</td>
</tr>
<tr>
<td></td>
<td>20.3%</td>
<td>13.5%</td>
<td>22.6%</td>
<td>20.5%</td>
<td>12.2%</td>
<td>10.9%</td>
</tr>
<tr>
<td>Occupation</td>
<td>Home maker</td>
<td>Skilled-labour</td>
<td>Non-professional job</td>
<td>Professional job</td>
<td>Total</td>
<td></td>
</tr>
<tr>
<td></td>
<td>95.9%</td>
<td>0.5%</td>
<td>3.6%</td>
<td>0.0%</td>
<td>100.0%</td>
<td></td>
</tr>
<tr>
<td>Physical Activity</td>
<td>Sedentary</td>
<td>Moderate</td>
<td>Heavy</td>
<td>Total</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>3.1%</td>
<td>95.1%</td>
<td>1.8%</td>
<td>100.0%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monthly per capita income in Rsx100</td>
<td>≤ 29</td>
<td>30 - 38</td>
<td>39 - 48</td>
<td>≥ 49</td>
<td>Total</td>
<td></td>
</tr>
<tr>
<td></td>
<td>26.75%</td>
<td>26.75%</td>
<td>22.6%</td>
<td>23.9%</td>
<td>100.0%</td>
<td></td>
</tr>
<tr>
<td>Gravity</td>
<td>Primi-gravida</td>
<td>Multi-gravida</td>
<td>Total</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>37.7%</td>
<td>62.3%</td>
<td>100.0%</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 2: Distribution of different dichotomous variables among study subjects.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Present (%)</th>
<th>Absent (%)</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Edema at baseline examination</td>
<td>45 (11.7)</td>
<td>340(88.3)</td>
<td>385(100.0)</td>
</tr>
<tr>
<td>Pallor at baseline examination</td>
<td>153(39.7)</td>
<td>232(60.3)</td>
<td>385(100.0)</td>
</tr>
<tr>
<td>H/O PIH in previous pregnancy</td>
<td>42(19.1)</td>
<td>178(80.9)</td>
<td>220(100.0)</td>
</tr>
<tr>
<td>H/O PIH in family (mother/sister)</td>
<td>29(7.5)</td>
<td>356(92.5)</td>
<td>385(100.0)</td>
</tr>
<tr>
<td>H/O hypertension in family member</td>
<td>202(52.5)</td>
<td>183(47.5)</td>
<td>385(100.0)</td>
</tr>
<tr>
<td>H/O Abortion</td>
<td>37(9.6)</td>
<td>348(90.4)</td>
<td>385(100.0)</td>
</tr>
</tbody>
</table>
Table 3: Distribution of continuous variables among study subjects.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Number</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Mean</th>
<th>Std. Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height (cm)</td>
<td>385</td>
<td>140</td>
<td>170</td>
<td>159.18</td>
<td>4.187</td>
</tr>
<tr>
<td>Age (years)</td>
<td>385</td>
<td>17</td>
<td>39</td>
<td>29.61</td>
<td>4.467</td>
</tr>
<tr>
<td>Monthly per capita income in Rsx100</td>
<td>385</td>
<td>11</td>
<td>115</td>
<td>40.35</td>
<td>16.182</td>
</tr>
<tr>
<td>Period of amenorrhea at baseline (weeks)</td>
<td>385</td>
<td>16</td>
<td>20</td>
<td>17.87</td>
<td>1.267</td>
</tr>
</tbody>
</table>

Table 4: Distribution of study subjects according to various risk factors.

<table>
<thead>
<tr>
<th>Variable</th>
<th>PIH</th>
<th>Total</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>1. History of PIH in past</td>
<td>Yes</td>
<td>32 (76%)</td>
<td>10 (24%)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>22 (12%)</td>
<td>156 (88%)</td>
</tr>
<tr>
<td>2. Family H/O PIH</td>
<td>Yes</td>
<td>21 (72%)</td>
<td>8 (28%)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>56 (16%)</td>
<td>300 (84%)</td>
</tr>
<tr>
<td>3. Family H/O hypertension</td>
<td>Yes</td>
<td>50 (25%)</td>
<td>152 (75%)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>27 (15%)</td>
<td>156 (85%)</td>
</tr>
<tr>
<td>4. Male gender of fetus</td>
<td>Yes</td>
<td>52 (24%)</td>
<td>162 (76%)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>25 (15%)</td>
<td>146 (85%)</td>
</tr>
<tr>
<td>5. Edema in early pregnancy</td>
<td>Yes</td>
<td>14 (%)</td>
<td>31(%)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>63 (%)</td>
<td>277(%)</td>
</tr>
<tr>
<td>6. Twin pregnancy</td>
<td>Yes</td>
<td>5 (83%)</td>
<td>1 (17%)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>72 (19%)</td>
<td>307 (81%)</td>
</tr>
</tbody>
</table>

Note: only those variables are shown which show statistically significant association.

Table 5: Distribution of PIH according to the age among study subjects.

<table>
<thead>
<tr>
<th>AGE</th>
<th>PIH</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>Number</td>
<td>77</td>
<td>308</td>
</tr>
<tr>
<td>Mean</td>
<td>31.06</td>
<td>29.25</td>
</tr>
<tr>
<td>Standard deviation</td>
<td>4.537</td>
<td>4.381</td>
</tr>
</tbody>
</table>

The mean age of study subjects with PIH was more than that of study subjects without PIH. 
\( t = -3.234, \ df = 383, \ p \ value = 0.001 \)
DISCUSSION

Pregnancy is a stressful state and if compounded by hypertension the potential for maternal and fetal adverse outcomes can be immense. PIH includes a group of hypertensive disorders developed due the gravid state after 20 weeks of gestation. It includes gestational hypertension, pre-eclampsia and eclampsia. Hypertensive disorders in pregnancy have been reported to occur as low as 0.51% to as high as 38.4%. PIH is a major public health problem all over India. Every pregnant woman was examined for blood pressure between 16 to 20 weeks of gestation at least once and enrolled in the study only if found normotensive, in order to fit in the definition of PIH and to rule out chronic hypertension.

Incidence of PIH increased with increasing age and was much higher among those study subjects who had a history of PIH in the previous pregnancy, who had a family H/O PIH, who delivered twins, who had a H/O hypertension in any family member, who had edema at baseline examination and who delivered male babies.

Incidence of PIH was much higher (76.2%) among those study subjects who had a history of PIH in the previous pregnancy as compared to those who had no such history (12.4%). H/O PIH in previous pregnancy has been shown an important risk factor of PIH in many other studies also. Jasovic-Siveska et al published a cross-sectional study in BMJ in Jan 2011 which showed that the pregnant females who have a history of PIH in past pregnancy have an increased risk of PIH in current pregnancy. Wikstrom et al. (2011) showed that H/O PIH in previous pregnancy was an important risk factor in the development of PIH in current pregnancy.

Incidence of PIH was much higher (72.4%) among those study subjects who had a Family H/O PIH as compared to those who had no such history(15.7%). Genetic studies have shown that daughters of women with a history of PIH are more susceptible to PIH than women in the general population. Familial predisposition for PIH has long been recognized. Single gene model and polygenic inheritance has been suggested. Some have reported an HLA-DR4 association with proteinuria in PIH. Polymorphisms of the genes for TNF, lymphotoxin-alpha and interleukin-1 have been studied with varying results.

Incidence of PIH was higher (24.8%) among those study subjects who had a H/O hypertension in any family member as compared to those who had no such history(14.8%). A study conducted by Zhao W, Wang JH et al (2004) showed that an increased incidence of PIH was seen in women with family history of Hypertension. Pierre Marie et al published a study in 2011 where they showed that the risk of development of PIH was much higher in women with a family history of hypertension (OR = 3.6) as compared to those without such a history. Incidence of PIH was higher (31.1%) among those study subjects who had edema at baseline examination as compared to those who had not edema (18.5%). Granger et al., 2001b has shown that in response to ischemic changes, various noxious substances are released from the placenta and decidua, these serve as mediators to provoke endothelial injury. Cytokines such as tumour necrosis factor-alpha (TNF-alpha) and interleukins contribute to increased capillary permeability which is responsible for the edema in pregnancy. They also suggested that if edema is present before 20 weeks of gestation then there is an increased chance of development of PIH, the same result as shown by our study.

Incidence of PIH was much higher (83.3%) among those study subjects who delivered twins as compared to those who delivered singlets (19.0%) in our study. This gives a relative risk of 4.3. Sibai BM and et al published a prospective cohort study in American Journal of Obstetrics and Gynecology in April 2000, where they showed that women with twin gestations had higher
rates of gestational hypertension (RR = 2.04) and preeclampsia (RR = 2.62)\textsuperscript{17}.

In our study the incidence of PIH increased with increasing age. Similar results have been shown by several studies. Fabio Parazzini et al have long back shown that the risk of developing PIH tended to increase with increase in maternal age. They showed that in comparison with women aged 20 – 25 years, the OR of having PIH was 3.5 (95% C I = 1.6 – 7.1) for women aged 26 – 30 years and 4.2 (95% C I = 1.9 – 8.8) for women aged > 30 years\textsuperscript{18}. A study conducted by Zhao W, Wang JH et al -2004 showed that age was related to PIH. An increased incidence of PIH was seen in women with increasing age\textsuperscript{14}.

Incidence of PIH was higher (24.3\%) among those study subjects who delivered male baby as compared to those who delivered female baby (14.6\%). P. Toivanen and T. Hirvonen published a study\textsuperscript{19} in the journal Science regarding the sex ratio of newborns in PIH. Their study showed a ratio of 1.24 males to females in 1061 babies born to mothers with PIH. The ratio increased as the severity of PIH increased, being 1.71 in cases in which the urinary output of protein was equal to or greater than 3 grams per 24 hours. Histo-incompatibility of the fetus and mother, including incompatibility due to an antigen (or antigens) dependent on the Y chromosome, has been suggested to function in this association\textsuperscript{20}.

There have been multiple studies on this topic, some showing the similar results and others showing no sex preponderance of males in PIH\textsuperscript{21,22,23,24}.

Chun Ye et al Published on Jun 2014, The 2011 Survey on Hypertensive Disorders of Pregnancy (HDP) in China: Prevalence, Risk Factors, Complications, Pregnancy and Perinatal Outcomes; where they have shown twin pregnancy, age of >35 years and family history of hypertension as important risk factors for the development of PIH, same results as that of our study\textsuperscript{25}.

CONCLUSION:

- PIH includes a group of hypertensive disorders developing due the gravid state after 20 weeks of gestation which include gestational hypertension, pre-eclampsia and eclampsia.
- Risk factors of PIH include increasing age, H/O PIH in past, family H/O PIH, family H/O hypertension, male gender of fetus, twin pregnancy and edema in early pregnancy.

RECOMMENDATIONS:

- Further research is needed to look for more and more risk factors of PIH, which can help further in its prevention.
- Awareness about PIH and its risk factors among females and health care workers must be generated so as to prevent its occurrence, lead to early diagnosis and management and prevent its progression and complications so that maternal and fetal outcome is improved.

DECLARATIONS

- Conflict of interest: none.
- Source of funding: none.
- Ethical approval: A clearance from the ethical committee of GMC Srinagar was sought before the study.
- Acknowledgement: I am extremely thankful to all the pregnant females who participated in this study for their cooperation.

REFERENCES


