Characteristics of vascular risk factor and the presence of ventriculomegaly among patients with white matter changes in Bangli General Hospital, Bali, Indonesia

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INTRODUCTION

White matter changes (WMC), often referred to as leukoaraiosis, is a radiological finding describing either white matter hypodensities on computed tomography (CT) or white matter hyperintensities on high signal changes on T-2 weighted magnetic resonance imaging (MRI), with the presumed origin of vascular impairment.1 WMC is a common finding among the elderly and this lesion is often accidentally found and rarely becomes the main focus of examination.2 However, the presence of such a lesion suggests a pathological process happening in the cerebral parenchyma.3

The Leukoaraiosis and Disability (LADIS) study found that populations with more severe degrees of WMC experienced worse declines in cognitive performance, executive function, motor control, attention, naming abilities, and visuconstructional abilities.4,5 Findings of this lesion are also associated with an increased risk of developing depression, which may result from the transition to disability. The LADIS study also found a relationship between the severity of WMC and the development of depressive symptoms based on the geriatric depression scale (GDS) examination, suggesting WMC as a causative factor.4,6

A data registry study shows that the highest prevalence of WMC occurs in patients aged 60 years and over.9 This finding supports the possibility of a pathological aging process that underlies the development of WMC. Such lesion highly correlates with the aging process, thus the term age-related white matter changes (ARWMC) exist.10 The aging process might cause microvascular and metabolic disturbances, thereby interfering with the perfusion of the brain parenchyma. These impairments as a risk factor are referred to as vascular risk factors (VRF).11 Dysregulation of blood pressure, such as hypertension and nocturnal blood pressure dipping disorder or metabolic disorders, such as dyslipidemia and type 2 diabetes mellitus, are common medical conditions found in elderly aged 60 years old and over.12,13 Those conditions are known to damage vascular, including in the brain parenchyma. Thus these conditions are considered VRF. VRF history shows a higher risk of developing WMC and cognitive impairment.5,14

In addition to vascular and metabolic disorders, aging causes degenerative disorders of the central nervous system structure. Dilatation of the ventricles

ABSTRACT

Background: White matter changes (WMC) is a common yet often incidental and neglected finding among older people in head CT or MRI examinations. This finding rarely becomes the main examination focus, although much research has proven its correlation with elderly disabilities, such as cognitive, executive, and motor function impairment. This lesion form is not fully understood, but chronic ischemic conditions may contribute due to a vascular risk factor (VRF) and periventricular cell impairment at the ventricular wall due to dilatation.

Methods: This research aimed to explore the characteristics of VRF (history of hypertension, diabetes mellitus, and dyslipidemia) and the presence of ventriculomegaly among patients with WMC finding on head CT examination. This research was conducted with a descriptive retrospective method using a data registry at Bangli General Hospital, Bali, Indonesia, in 2022.

Result: From 97 patients with WMC findings, most were aged >60 (77.30%). Ventriculomegaly was found in 33.00% of them. Almost all had a history of hypertension (92.80%), and a history of dyslipidemia was found in 61.9%. Of all VRF components, diabetes mellitus was the least frequently found in patients (19.60%). The majority of WMC lesions involved the periventricular structure.

Conclusion: WMC finding was more frequent among patients aged >60, with a history of hypertension being the most frequent compared to other components of VRF. Ventriculomegaly was found in one-third of them.

Keywords: Vascular risk factor, ventriculomegaly, white matter changes.


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(ventriculomegaly) is among the most common findings in the elderly. When the ventricles are dilated, the walls of the ventricles, composed of ependymal cells, might be damaged. This can cause interference with the exchange process and potentially cause accumulation of toxic metabolites and reduced nutrient supply to the cerebral parenchyma. This is consistent with the findings of previous studies, which stated that an increase in the area of lateral ventriculomegaly is related to an increase in the area of WMC in the periventricular area.

Although the WMC findings are important and should not be neglected, studies on this matter, especially in the Indonesian region, are still lacking. We tried to provide empirical data regarding the characteristics of patients with WMC based on age, history of VRF, and findings of ventriculomegaly.

METHODS

This research aimed to explore the characteristics of VRF (history of hypertension, diabetes mellitus, and dyslipidemia) and ventriculomegaly among patients with WMC finding on head CT examination. This research was conducted with a descriptive cross-sectional method using a data registry at Bangli General Hospital, Bali, Indonesia. The sampling technique used in this study was total population sampling. This study has been approved by the Ethic Committee for Public Health, Bangli General Hospital.

Patients

In our hospital, patients with indications for radiological head CT imaging examinations are listed, whether or not due to coexisting clinical conditions. In total, 990 patients underwent head CT examinations in January-August 2022. We performed a chart and data registry review on all of those patients. Patients with incomplete identity and clinical and radiologic data information are excluded.

Computed Tomography Examination

Data on the presence of WMC and ventriculomegaly were acquired from the history of head CT, which was performed using a 16-slice machine (BrightSpeed 16; GE Healthcare). For each patient, 16-slice CT scan images were applied. Due to availability in our hospital, CT scan recordings were assessed independently by 1 radiologist without blinding to clinical and grouping information. Any presence of white matter hypodensities supporting a description of WMC, regardless of the size and location, was noted visually. In this study, we did not determine the severity of WMC. Patients with WMC findings were further included in the study. Any presence of ventriculomegaly was also assessed. We assessed the presence of cerebral atrophy in relation to hydrocephalus ex vacuo in patients with ventriculomegaly findings.

Vascular Risk Factor

The history of VRF was acquired through the medical records of the patients. Patients with a history of elevated systolic and/or diastolic pressure (>140 mmHg for systolic pressure and >90 mmHg for diastolic pressure) were considered hypertensive. Diabetes mellitus was considered when there was a finding of elevated hemoglobin A1C (HbA1C), blood fasting glucose, and/or postprandial blood glucose (>6.5%, >126 mg/dL, and >200 mg/dL, respectively). Dyslipidemia was considered when there was a history of elevated low-density lipid (LDL) and/or triglyceride (TG) (>2.6 mmol/L and >1.70 mmol/L, respectively). A history of prior diagnosis or prior history of medication for these conditions was also considered for respective conditions.

Data Analysis

Data were computed and analyzed using computing software (SPSS, version 11.0; SPSS Inc). Univariate analysis was conducted on data regarding age, sex, findings of ventriculomegaly, and history of hypertension, diabetes mellitus, and dyslipidemia. We also analyze systolic and diastolic pressure, cerebral atrophy, and the location of WMC findings as additional data. Cross-tabulation analysis was conducted between age and other variables, such as findings of ventriculomegaly and VRFs. Results of the data analysis were presented as descriptive statistics, including mean, SD, frequency, and percentage and are shown with tables and charts.

RESULTS

Of the 990 patients who underwent head CT examinations, WMC was found in 103 of them. After exclusion, we included 97 patients. As seen in Table 1, we found that the majority were men aged >60 years. However, the disparity in WMC findings between men and women is not too great (3% difference). We also found that the youngest age of the overall population is 15 years old, and the oldest age of the population is 98 years old. Patients aged 15 years old are patients with a history of epilepsy with possible congenital cerebral defects. We did not find any WMC located merely in the centrum semiovale. Most WMC findings were confined to the periventricular (73.20%) or involved the centrum semiovale structures (25.80%).

Hypertension is the most common VRF component we encountered in the population (92.8%). As can be seen from Table 2, we found that the mean systolic and diastolic blood pressure of the patients with hypertension at the time of first contact with healthcare workers at the hospital was higher than the population without hypertension. In the population, we also found systolic and diastolic pressure measurements included in the hypertension criteria despite being below the operational definition of the hypertension variable in the inclusion criteria. This is because the patients had previously been diagnosed with hypertension and regularly took antihypertensive drugs. Thus, the measurement of blood pressure can be normal.

From Figure 2, we can see that the measured ventricular structures in most patients did not experience dilation. We found that the majority of subjects with ventriculomegaly also had cerebral atrophy (78.1%).

Through cross-tabulation analysis of VRF and age, we found that the entire population in the age group of 50-59 years old had a history of hypertension. We also found a history of dyslipidemia was lower in the age group of <50 years, but more dyslipidemia was found in the age group of >50 years. From the results of a cross-tabulation analysis of ventriculomegaly findings and age, we also found that
Table 1. Demographic Data

<table>
<thead>
<tr>
<th>Demography</th>
<th>WMC finding (n=97) (%)</th>
<th>Statistics (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (M/F)</td>
<td>50/47 (51.50/48.50)</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;50 years old</td>
<td>8 (8.25)</td>
<td>43.38±11.72</td>
</tr>
<tr>
<td>50-59 years old</td>
<td>14 (14.45)</td>
<td>56.21±2.52</td>
</tr>
<tr>
<td>&gt;60 years old</td>
<td>75 (77.30)</td>
<td>73.93±9.02</td>
</tr>
</tbody>
</table>

Note: WMC finding values expressed as n(%), statistics values expressed as mean ± SD. Abbreviation: M=male; F=female; WMC=white matter changes.

Ventricles that were not dilated were more common in all age ranges.

**DISCUSSION**

WMC or leukoaraiosis of the cerebral parenchyma is a radiological finding in the form of a patchy or diffuse hypodense area in the cerebral white matter on head CT examination or a hyperintense appearance on T2-weighted MRI involving the periventricular area and/or centrum semiovale with the presumed origin of vascular impairment. The prevalence of WMC in the prior studies that have been carried out showed various results.  

WMC is associated with the aging process. This process might cause changes in the anatomy and physiology of the body which may have the potential to develop further into being a risk factor for the appearance of this lesion, such as vascular disorders (hypertension, blood pressure dysregulation) and metabolic disorders (hyperlipidemia, diabetes). A registry study conducted in Japan in 2021 found that the prevalence of WMC on MRI examination increased with age. The WMC findings in this study are similar, where we found that the WMC findings in the age group >60 years were higher compared to the age group 50-59 years, and the difference was even greater in the age group <50 years.

The aging process increases the risk of developing VRF in patients, where there will be disturbances in both the vascular and metabolic systems. This group of risk factors includes hypertension, diabetes mellitus, and dyslipidemia. We found that hypertension was the most common component of VRF in patients with WMC findings, followed by dyslipidemia. The data tabulation found that the percentages of history of hypertension, dyslipidemia, and diabetes mellitus in the total population were respectively 92.8%, 61.9%, and 19.6%. This finding is similar to a study conducted by Maillard P et al., where the most common VRF component found in patients with results of WMC lesion was a history of hypertension of 80.2%, followed by a history of dyslipidemia (71.1%) and a history of diabetes mellitus being the component of VRF that was the least frequently found (35.5%).

Previous studies have found that hypertension is one of the most prevalent risk factors for WMC. Chronically elevated blood pressure is an independent contributor to WMC findings and progression. Hypertension’s severity in systolic, diastolic, and pulse pressure measurements correlates with increased WMC volume. We found that the mean systolic and diastolic pressures of the total population of subjects with WMC lesions were above the threshold for hypertension in this study (>140 mmHg systolic pressure and >90 mmHg diastolic).

In this study, 80.4% of patients with WMC findings did not have diabetes mellitus. The relationship between diabetes mellitus and WMC findings are still unclear. A cross-sectional study by van Harten B et al. found a relationship between type 2 diabetes mellitus and WMC in the subcortical region. The effect of glycemic blood levels on WMC volume was also found in a study of an elderly population without dementia, where HbA1c levels positively correlated with subcortical WMC.

Apart from VRF, the aging process is also associated with dilatation of the ventricular system. Degenerative processes of the central nervous system may cause it. Dilatation of the ventricles is one of the most common findings in the elderly. The ventricles themselves are the site for cerebrospinal fluid (CSF) movement, which is rich in nutrients to enter the cerebral parenchyma, as well as the places of toxic metabolites removal from the parenchyma.
Table 2. **Blood pressure measurement**

<table>
<thead>
<tr>
<th>Hypertension</th>
<th>Measurement</th>
<th>Systolic (mmHg)</th>
<th>Diastolic (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of hypertension</td>
<td></td>
<td>169.40±26.17</td>
<td>99.08±15.31</td>
</tr>
<tr>
<td>No History of hypertension</td>
<td></td>
<td>117.14±4.88</td>
<td>78.57±3.78</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>165.63±28.66</td>
<td>97.60±15.70</td>
</tr>
</tbody>
</table>

Note: Values expressed as mean + SD.

Figure 2. Pie chart of ventriculomegaly distribution. Note: Chart values are expressed as n (%). Abbreviation: VM=ventriculomegaly.

Table 3. **Cross tabulation result**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Age Group</th>
<th>50-59 years old</th>
<th>&gt;60 years old</th>
</tr>
</thead>
<tbody>
<tr>
<td>VRF</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HT</td>
<td></td>
<td>7 (87.50)</td>
<td>14 (100.0)</td>
</tr>
<tr>
<td>DM</td>
<td></td>
<td>1 (12.50)</td>
<td>3 (21.40)</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td></td>
<td>3 (37.50)</td>
<td>10 (71.40)</td>
</tr>
<tr>
<td>Ventriculomegaly</td>
<td></td>
<td>2 (25.0)</td>
<td>2 (14.30)</td>
</tr>
</tbody>
</table>

Note: Values expressed as n (%). Abbreviation: VRF=vascular risk factor; HT=hypertension; DM=diabetes mellitus.

In this study, we found that most WMC lesions involved the periventricular. Of the 32 findings of ventriculomegaly, 25 subjects (78.1%) supported the hydrocephalus ex vacuo description, in which communicating hydrocephalus accompanied by generalized cerebral atrophy was present. Previous studies have found that processes of leaking CSF components into the periventricular area due to disruption of the ependymal wall still occurred in cases of ventriculomegaly without any compression of the cerebral parenchyma. This is evident from the prior study, where there were no significant differences in the findings of WMC lesions in the periventricular and subcortical areas between patients with idiopathic normal pressure hydrocephalus (iNPH) and hydrocephalus ex vacuo patients, considering the different process of ventricular dilation in these two conditions.

Our study, however, is not without limitations. We examined the presence of WMC using CT, where MRI is the gold standard in diagnosing. Although CT and MRI performance in visualizing medium to bigger size lesions are similar, smaller lesions might not be visible in our patients, therefore potentially decreasing the number of included patients. We also did not consider the degree of severity of WMC lesions and hypertension in the calculation. In addition, we did not exclude other conditions that may influence the presence or pattern of the lesion, such as the history of infarctions, hemorrhages, and other brain conditions. To bypass this limitation, further studies may use better modalities that visualize these lesions better, even using perfusion imaging modalities. Conditions that may interfere with the lesion also need to be considered.

This is an empirical study regarding the characteristics of VRF and ventriculomegaly in patients with WMC findings on head CT examination. We found that most of those patients had a history of hypertension. Ventriculomegaly was found in one-third of those patients, and most of them support the description of hydrocephalus ex vacuo.

**CONCLUSION**

WMC finding was more frequent among patients aged >60, with a history of hypertension being the most frequent compared to other components of VRF. Ventriculomegaly was found in one-third of them.
CONFLICT OF INTEREST
The authors declare that there is no competing interest regarding the manuscript.

ETHICAL CONSIDERATION
This research was conducted based on the ethical conduct of research from the Ethics Committee of Bangli General Hospital.

FUNDING
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AUTHOR CONTRIBUTION
All authors contributed to the study from the conceptual framework, data gathering, and analysis until the study’s results were interpreted upon publication.

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REFERENCES