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# Prevalence of Risk Factors in Patients With Spontaneous Intracerebral Hemorrhage in Damascus_Syria: A Retrospective Cross-Sectional Study

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## ABSTRACT

**Objectives:** This study aims to determine the prevalence of risk factors among patients with spontaneous intracerebral hemorrhage in Syrian society.

**Methods:** This study is a retrospective cross-sectional study, patients' data were collected from four hospitals. Cross-tabulation tables and the $\chi^2$ test were used to show the relationship between gender/age and the prevalence of risk factors, demonstrate statistical significance, and calculate $p$ value.

**Results:** From a total of 194 patients included in the study, there were 123 males, accounting for 63.4% of the patients, while there were 71 females, accounting for 36.6%. The most common risk factor among intracerebral hemorrhage patients was hypertension at 44.8% of the total patients, followed by antithrombotic use at 25.8%, smoking at 19.1%, diabetes at 15.5%, and hematological diseases making up 9.3% of the patients, whereas in age groups under 10 years, various hematological diseases were the most prevalent risk factors at 42.5%, followed by prematurity at 27.5%, and hyaline membrane disease at 15%. The study showed no statistically significant differences in the distribution of risk factors between males and females except for smoking. However, the results revealed a significant difference in the distribution of risk factors according to age for Smoking, hypertension, antithrombotic use, diabetes, arteriovenous malformation, hyaline membrane disease, hematological diseases, and prematurity ($p < 0.05$).

**Conclusion:** The study showed that hypertension and antithrombotic use are the most important risk factors for intracerebral hemorrhage, so controlling arterial pressure and periodic tests such as platelet count/PT/PTT are gold roles in preventing intracerebral hemorrhage.

## 1 | Introduction

Intracerebral hemorrhage (ICH), a specific type of stroke, represents a serious medical condition characterized by the formation of a hematoma within the brain parenchyma, which may or may not extend into the ventricles [1]. Although ICH has a complex pathophysiology, it can be divided into two sections: primary and secondary intracerebral hemorrhage. ICH may arise as a complication associated with pre-existing conditions, such as vascular malformations or tumors, and is classified as secondary intracerebral hemorrhage. In contrast, primary intracerebral hemorrhage occurs in the absence of a distinct underlying lesion and represents the most common form of ICH [2]. The primary mechanism of injury in ICH involves the compression of brain parenchyma due to the mass effect of the hematoma, leading to structural disruption of the parenchymal architecture [3].

ICH comprises 15%–20% of all stroke cases, with an annual incidence rate estimated at 24.3/100,000 individuals. The associated disability rate can be as high as 75%. The highest incidence rates are observed in individuals aged 50–59 and 60–69 years. Annually, ~2.8 million deaths worldwide are attributed to ICH [4–6]. In South Korea, ICH ranks as the second leading cause of death after cancer and is the primary cause of mortality related to a single organ disease [7].

Non-contrast computed tomography (NCCT) is a rapid imaging technique known for its high sensitivity in detecting acute ICH. Due to its widespread availability, NCCT is regarded as the gold standard for diagnosing this condition [8].

The outcomes of ICH exhibit significant variability, influenced by factors such as hematoma volume, location, extension into the ventricles, and other clinical variables [3]. Hematoma expansion is associated with increased mortality rates and greater long-term functional dependence. In young adult patients with ICH, both low and high hemoglobin levels at the time of admission have been correlated with unfavorable outcomes; survival analyses indicate that even mild to moderate anemia is linked to elevated mortality [9, 10].

Modifiable risk factors for ICH include hypertension, tobacco use, excessive alcohol intake, reduced levels of low-density lipoprotein cholesterol, low triglycerides, and the use of certain medications, such as antithrombotic agents and sympathomimetics. In contrast, nonmodifiable risk factors encompass advanced age, male gender, cerebral amyloid angiopathy (CAA), and Asian ethnicity [3]. Some studies report the following prevalence rates of risk factors among patients with spontaneous ICH: hypertension 78.7%, smoking 13.1%, dyslipidemia 8.1%, diabetes mellitus 6.6%, renal insufficiency 4.1%, anticoagulant drugs use 4.1% [11–13].

Hypertension is a well-established risk factor for ICH, with primary ICH frequently associated with chronic hypertensive conditions. Pathologically, hypertension contributes to arteriolosclerosis, characterized by the accumulation of degenerative materials within the tunica intima of arterial walls. This condition manifests through fibrinoid necrosis, lipohyalinosis, microatheroma formation, and the presence of microaneurysms [14–16].

The most common clinical manifestation of CAA is acute lobar ICH. The term "lobar" refers to the location in the cortex and subcortical white matter of a hemispheric lobe of the brain; this contrasts with the deep locations, such as putamen, thalamus, and pons, which are characteristic of hypertensive hemorrhage. The clinical presentation of CAA-related hemorrhage varies with the lesion size and brain region impacted. Lobar hemorrhages can cause hemiparesis from the involvement of pyramidal motor neurons and tracts. A large lobar hemorrhage may cause depressed consciousness from direct involvement or secondary mass effect on reticular activating system networks. In comparison, smaller lobar or cerebellar hemorrhages may cause more limited focal deficits related to the underlying brain structure impacted [17]. Findings show that although patients with CAA were at high risk of recurrent hemorrhage after surgery, the mortality rate was relatively low despite the severity of lobar ICH [18].

Elevated alcohol consumption is a significant contributor to the onset of liver diseases, and it may also exacerbate hypertension. Furthermore, alcohol intake has been linked to alterations in the coagulation system, potentially compromising the integrity of cerebral blood vessels [19]. A reduced glomerular filtration rate (GFR) is a significant risk factor for hemorrhagic stroke, while its association with ischemic stroke remains less clear. Among the various mechanisms contributing to cerebrovascular disease, small vessel microangiopathy is likely the most closely linked to chronic kidney disease (CKD), as both conditions are thought to stem from increased endothelial permeability due to elevated blood flow in low-resistance end-arterial regions, such as the brain and kidneys [20, 21].

Current smoking and diabetes mellitus have been identified as relatively weak risk factors for stroke, with inconsistent findings reported regarding hypercholesterolemia. Nonetheless, low levels of cholesterol may increase the susceptibility of blood vessels to rupture, given the role of cholesterol in maintaining membrane fluidity [22, 23].

Spontaneous ICH constitutes ~50% of strokes in pediatric populations, compared to about 15% in adults. Previous research indicates that premature infants requiring assisted ventilation are at a heightened risk for developing intracranial hemorrhage [24, 25].

The prevalence of major modifiable risk factors for ICH can change rapidly. Enhancing our understanding of the risk factors associated with spontaneous intracerebral hemorrhage (sICH) has the potential to improve patient prognoses [26, 27], to this reasons this study has a great importance.

## 2 | Methods

An ethical approval was obtained from the Biomedical Research Ethics Committee (BMREC) at Damascus University, with the ID Number MD-020624-243. Additionally, approvals were secured from the relevant hospital administrations. All patients included in the study were thoroughly informed of the authors' intent to access their medical records, and verbal consent was obtained via telephone contact.

This investigation is a retrospective cross-sectional study. Patient data were collected by reviewing the medical records of individuals diagnosed with ICH at Al-Assad University Hospital, Al-Mouwasat University Hospital, Children's University Hospital, and Damascus Hospital. Diagnosis was confirmed through CT scans without contrast or brain echography for newborns admitted to the Children's University Hospital. Patients with uncertain diagnoses of ICH, incomplete medical records, or missing CT scan reports were excluded from the study, as were those diagnosed with traumatic ICH.

Data were recorded using Microsoft Excel, encompassing variables such as age, gender, and various potential risk factors including smoking, alcohol consumption, hypertension, antithrombotic use, diabetes, CKD, primary and secondary tumors, aneurysms, moyamoya disease, arteriovenous malformations (AVMs), prematurity, hyaline membrane disease, and hematological disorders. This information was gathered through comprehensive medical and drug histories.

Data analysis was performed using IBM SPSS Statistics. Cross-tabulation tables were employed to illustrate the relationships between gender/age and the prevalence of risk factors. The $\chi^2$ test was utilized to assess statistical significance and calculate $p$ values, with all statistical analyses conducted at a confidence interval of 95% (CI: 95%) and a significance level of $p < 0.05$. Microsoft Excel was also utilized to create tables and figures for data presentation.

## 3 | Results

A total of 194 patients were included in the study, comprising 123 males (63.4%) and 71 females (36.6%). The age distribution of the patients was as follows: 40 patients were under the age of 10 (20.6%), 16 patients were aged 11–30 (8.2%), 72 patients were aged 31–60 (37.1%), and 66 patients were over the age of 60 (34%), as illustrated in Figure 1.

Among the patients with ICH, 38 (19.6%) had no known risk factors. Those with one risk factor numbered 77 (39.7%), while 47 patients (24.2%) had two risk factors, 27 patients (13.9%) had three risk factors, and 5 patients (2.6%) had four risk factors.

Hypertension was identified as the most prevalent risk factor, affecting 44.8% of the total patient population, followed by antithrombotic use at 25.8%, smoking at 19.1%, diabetes (both Types I and II) at 15.5%, and hematological disorders—including bacteraemia, disseminated intravascular coagulation (DIC), hemophilia, hemorrhagic disease in newborns, and leukemias—accounting for 9.3%. Other risk factors such as alcohol consumption, CKD, aneurysms, AVMs, moyamoya disease, prematurity, hyaline membrane disease, and tumors were present in fewer patients, as shown in Figure 2.

Statistical analysis indicated no significant differences in the distribution of risk factors between males and females ($p > 0.05$). However, a significant difference was observed in the prevalence of smoking among the patients, with 24.4% of males and 9.9% of females identified as smokers ($p < 0.05$). Hypertension, antithrombotic use, smoking, and diabetes were consistently the most prevalent risk factors across both genders. The distribution of risk factors by gender is illustrated in Table 1 and Figure 2.

The study also revealed significant differences in the distribution of risk factors according to age for smoking, hypertension, antithrombotic use, diabetes, AVMs, hyaline membrane disease, hematological diseases, and prematurity ($p < 0.05$). Conversely, alcohol consumption, CKD, tumors, moyamoya disease, and aneurysms did not demonstrate statistically significant associations with age ($p > 0.05$). The distribution of risk factors by age among patients with ICH is presented in Table 2 and Figure 3.

In the age group of 31–60 years, hypertension was the most prevalent risk factor at 58.3%, followed by smoking at 23.6% and antithrombotic use at 22.2%. In the group over 60 years, hypertension continued to be the leading risk factor at 68.2%, followed by antithrombotic use at 47% and smoking at 24.2%. Among patients under the age of 10, various hematological diseases were the most common risk factors, accounting for 42.5%, followed by prematurity at 27.5% and hyaline membrane disease at 15%.

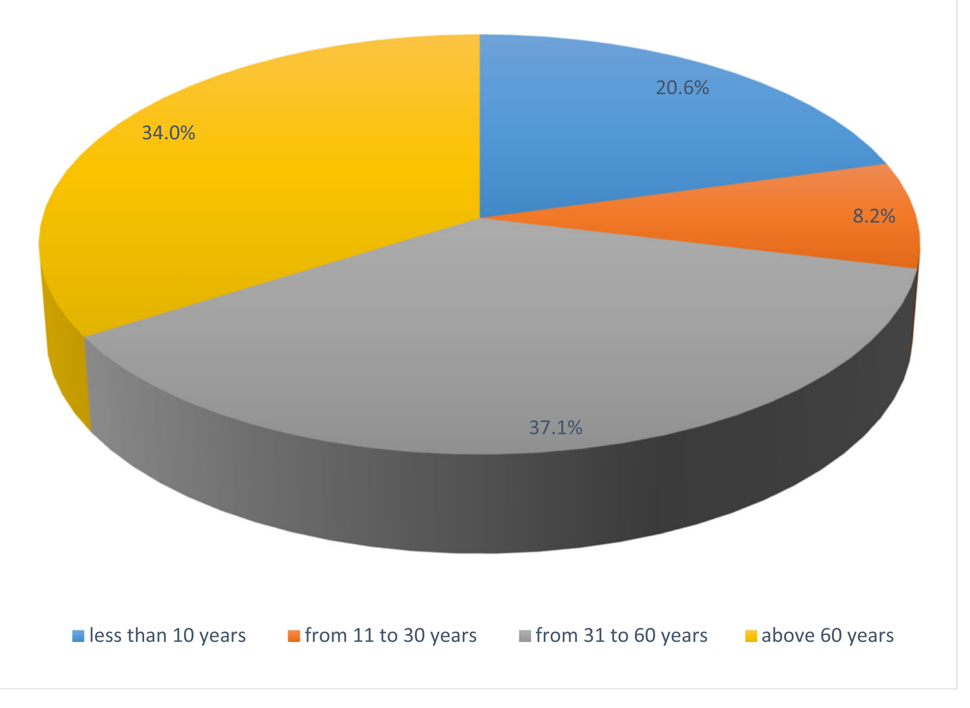


**FIGURE 1** | Distribution of intracerebral hemorrhage according to age.

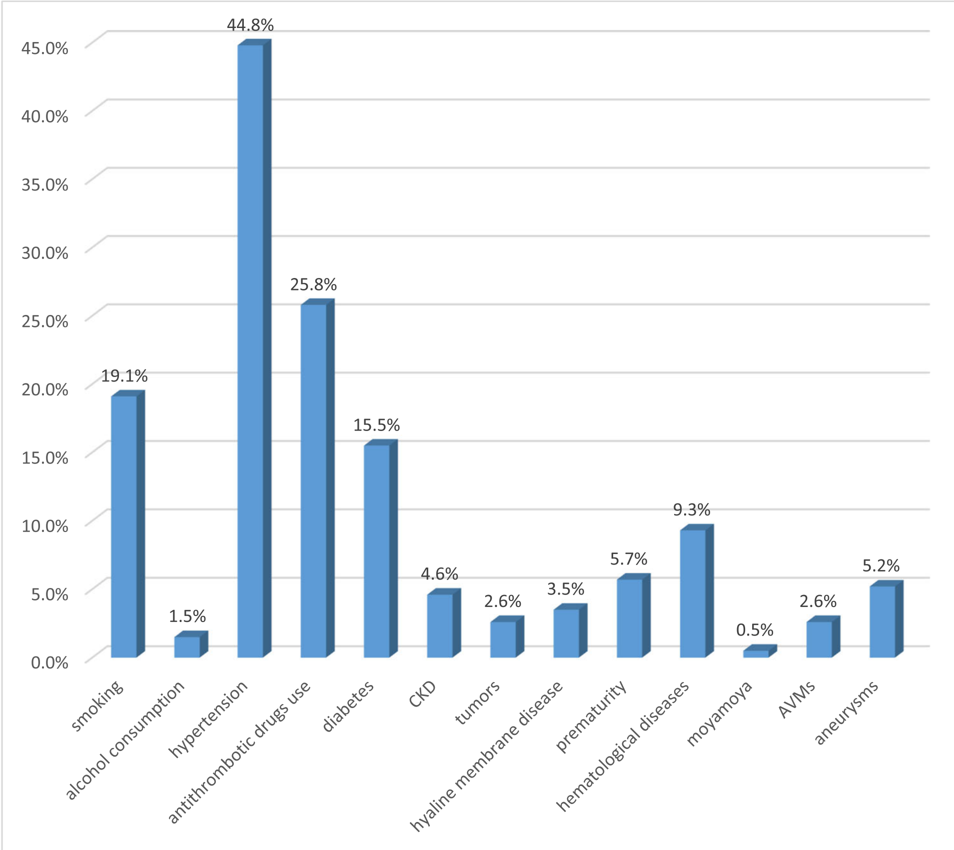


**FIGURE 2** | Prevalence of risk factors in all patients.

**TABLE 1** | Distribution of risk factors according to gender.

| | Count ($N = 194$) | | Percentage (%) | | |
|---|---|---|---|---|---|
| **Risk factors** | **Male** | **Female** | **Male** | **Female** | ***p*** |
| Smoking | 30 | 7 | 24.4 | 9.9 | $p < 0.05$ |
| Alcohol consumption | 3 | 0 | 2.4 | 0 | $p > 0.05$ |
| Hypertension | 57 | 30 | 46.3 | 42.3 | $p > 0.05$ |
| Antithrombotic drugs use | 35 | 15 | 28.5 | 21.1 | $p > 0.05$ |
| Diabetes | 22 | 8 | 17.9 | 11.3 | $p > 0.05$ |
| CKD | 7 | 2 | 5.7 | 2.8 | $p > 0.05$ |
| Tumors | 3 | 2 | 2.4 | 2.8 | $p > 0.05$ |
| Hyaline membrane disease | 3 | 3 | 2.4 | 4.2 | $p > 0.05$ |
| Prematurity | 6 | 5 | 4.9 | 7 | $p > 0.05$ |
| Hematological diseases | 13 | 5 | 10.6 | 7 | $p > 0.05$ |
| Moyamoya | 0 | 1 | 0 | 1.4 | $p > 0.05$ |
| AVMs | 3 | 2 | 2.4 | 2.8 | $p > 0.05$ |
| Aneurysms | 5 | 5 | 4.1 | 7 | $p > 0.05$ |

## 4 | Discussion

This is the first study of its kind in Syria to determine the distribution of ICH according to age and gender. We were keen to study the distribution of risk factors among all age groups including children and adults. There have been several publications on the hemorrhagic strokes; however, we aimed to determine the risk factors for spontaneous ICH in a Syrian population.

The salient findings of our study were as follows:

1. The most common risk factor in all ages and especially more than 30 years is hypertension at 44.8%

**TABLE 2** | Distribution of risk factors according to age.

| | Less than 10 years | From 11 to 30 years | From 31 to 60 years | Above 60 years | p |
|---|---|---|---|---|---|
| Smoking | 0.0% | 25.0% | 23.6% | 24.2% | $p < 0.05$ |
| Alcohol consumption | 0.0% | 0.0% | 2.8% | 1.5% | $p > 0.05$ |
| Hypertension | 0.0% | 0.0% | 58.3% | 68.2% | $p < 0.05$ |
| Antithrombotic drugs use | 5.0% | 6.3% | 22.2% | 47.0% | $p < 0.05$ |
| Diabetes | 0.0% | 0.0% | 22.2% | 21.2% | $p < 0.05$ |
| CKD | 0.0% | 0.0% | 6.9% | 6.1% | $p > 0.05$ |
| Tumors | 2.5% | 6.3% | 1.4% | 3.0% | $p > 0.05$ |
| Hyaline membrane disease | 15.0% | 0.0% | 0.0% | 0.0% | $p < 0.05$ |
| Prematurity | 27.5% | 0.0% | 0.0% | 0.0% | $p > 0.05$ |
| Hematological diseases | 42.5% | 0.0% | 0.0% | 1.5% | $p < 0.05$ |
| Moyamoya | 0.0% | 0.0% | 0.0% | 1.5% | $p > 0.05$ |
| AVMs | 0.0% | 18.8% | 1.4% | 0.0% | $p < 0.05$ |
| Aneurysms | 2.5% | 6.3% | 9.7% | 1.5% | $p > 0.05$ |

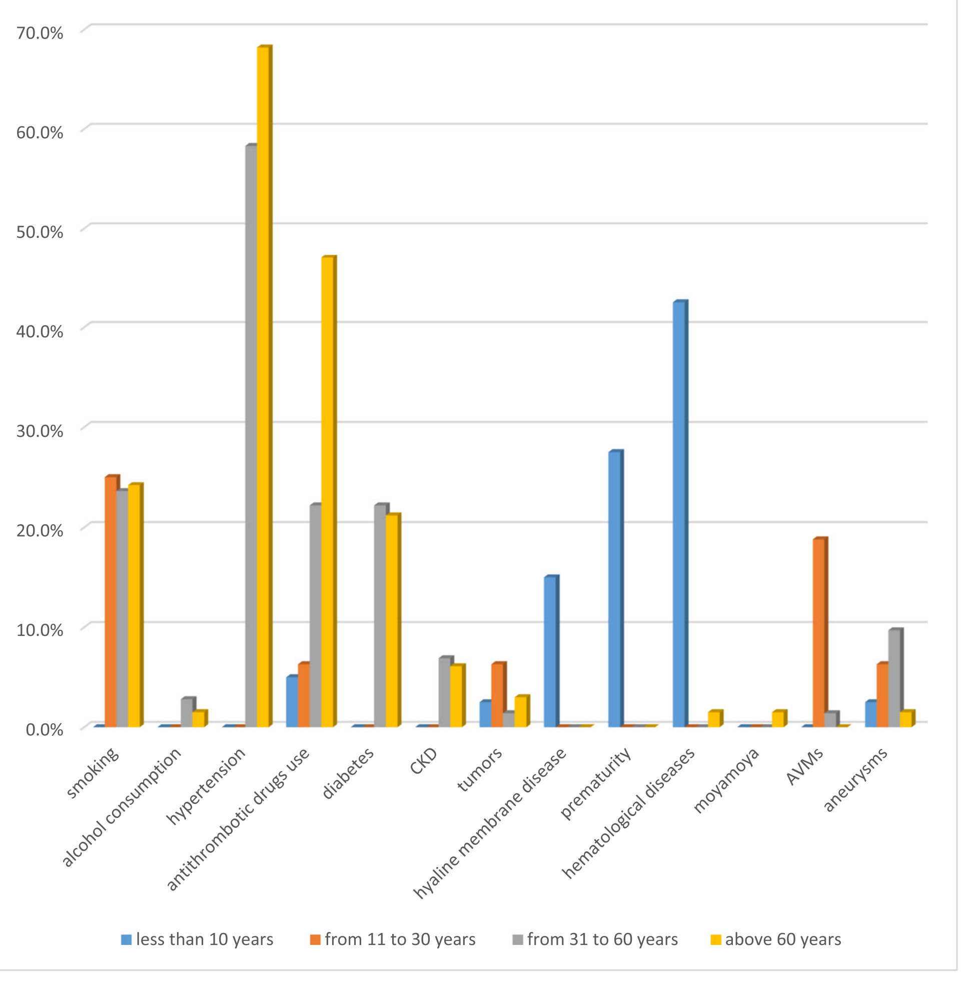


**FIGURE 3** | Distribution of risk factors according.

of the total patients, followed by antithrombotic use at 25.8%.

2. The most common risk factor in age < 10 years is hematological diseases.
3. The most common risk factors from 11 to 30 years are smoking and AVMs.
4. We also observed a peak in injury occurrence among newborns, especially in premature infants, which is a prominent result that was not indicated by previous studies.

Age is widely recognized as a critical immutable risk factor for spontaneous ICH. Research by Ariesen and colleagues, Sturgeon and colleagues, and Efstathiou and colleagues has consistently identified advanced age as a significant contributor to the incidence of ICH [22, 28]. In the present study, 66 patients over the age of 60 accounted for 34%.

Additionally, male sex, particularly in individuals over 55 years of age, has been identified as another risk factor for spontaneous ICH. While the meta-analysis conducted by Ariesen and colleagues supports this association, Sturgeon and colleagues and Efstathiou and colleagues did not find a corresponding link in their findings [22, 28, 29]. Gender was in favor of males in our study group.

There were 123 males, accounting for 63.4% of the patients, but our study showed no statistically significant differences in the distribution of risk factors between males and females except for smoking, which was higher among males. Contrastingly, a population-based study in France indicated that smoking prevalence remained stable among men and women aged 15–75 during the study period, although it did show an increase among women aged 50–75 years [30]. The existing literature has established that cigarette smoking not only elevates the risk of spontaneous ICH but also exacerbates hematoma expansion, leads to poorer clinical outcomes, and increases mortality associated with ICH [31]. In our study, smoking was a risk factor in 19.1% as in the study of Asuman Celikbilek et al. was found in 17% [32].

The role of hypertension in the etiology of spontaneous ICH has been emphasized in the literature, including studies by Sacco, Ariesen and colleagues, and Woo and colleagues [33, 34]. In one study with 152 cases, hypertension was found in 73% of patients [35]. In another series involving 141 patients, hypertension was determined in 83% of patients [36]. In our study group, hypertension was determined hypertension at 44.8% of the total patients especially more than 30 years.

This finding underscores the critical importance of blood pressure management in both the prevention and treatment of ICH. A recent investigation by the Antihypertensive Treatment of Acute Cerebral Hemorrhage II Study Group has validated the effectiveness and safety of early and aggressive antihypertensive therapy. This study provided compelling evidence that significant reductions in systolic blood pressure can mitigate hematoma expansion in patients experiencing spontaneous ICH [37].

In patients aged 11–30 in our study, smoking and AVMs were the most important factors, these findings align with those of Ruíz-Sandoval and colleagues, who assessed a cohort of 200 patients aged 15–40 years and reported that tobacco use was the most prevalent risk factor, affecting 20% of participants [38].

For results in children under 10 years in this study the most risk factors were hematological diseases 42.5% (such bacteraemia, DIC, hemophilia, hemorrhagic disease in the newborn, and leukemias) followed by prematurity at 27.5%, and hyaline membrane disease at 15%; while a systematic review adhering to PRISMA guidelines, which analyzed data from 7931 children and adolescents, identified vascular etiologies as the most common cause of spontaneous intracranial hemorrhages in the pediatric population ($n = 1727$, representing 43.08% of all identified causes). Among these vascular causes, AVMs were the most frequently reported, comprising 70.99% of all vascular-related incidents ($n = 1226$) [39].

The pathophysiology of ICH varies significantly among populations with hematological diseases, necessitating distinct therapeutic strategies and influencing clinical outcomes. The underlying mechanisms contributing to ICH in these patients may involve abnormalities in platelet count or function, various coagulation disorders, hyperleukocytosis, sepsis, and structural anomalies in blood vessel walls [40].

The primary objective following the diagnosis of ICH is to reduce the likelihood of rebleeding and prevent hematoma expansion within the initial 24–72 h. This involves promptly addressing any coagulation abnormalities present, which includes correcting known factor deficiencies and reversing the effects of anticoagulant medications with the assistance of hematology specialists. For patients on vitamin K antagonists, current guidelines for managing spontaneous ICH recommend achieving an international normalized ratio (INR) of < 1.4 through the administration of fresh frozen plasma (FFP), vitamin K, prothrombin complex concentrates, and newer agents such as recombinant activated factor VIIa [39]. Research is ongoing to establish definitive criteria for platelet transfusions in patients receiving antiplatelet therapy. Nevertheless, preliminary analyses from smaller case series indicate that those who received platelet transfusions within 12 h post-ictus exhibited a reduction in the final size of the ICH [41].

We also observed ICH occurrence in patients without any risk factors (19.6%), perhaps these patients need more monitoring and attention until we know their risk factors for cerebral hemorrhage.

This study has some potential limitations. First, the sample size is relatively small, mainly due to the fact that the participants were selected from four hospitals in Damascus only, so this study must be expanded to the rest of the cities to obtain more accurate results that represent the entire Syrian society. Second, despite the serial high measurements of blood pressure and serum glucose levels in follow-up, hypertensive or diabetic conditions still might be masked because of low blood pressure or serum glucose measurements on admission during the acute phase. Third, it might be the paucity of discharge data and absence of advanced imaging.

## 5 | Conclusion

The study showed that hypertension is an important factor for ICH and is the most common risk factor, which makes controlling arterial pressure an important role in preventing ICH, we also found a high incidence rate among those taking antithrombotics, so they must be taken carefully to the extent required, while conducting periodic tests such as (platelet count/PT/PTT). In addition, abstaining from smoking plays an important role in the primary prevention of ICH, as it is the third most common risk factor.

The results of the study indicated that 19.1% of patients with ICH had no known risk factors, which encourages further investigation into other potential risk factors that may increase the likelihood of ICH, or into additional risk factors that might be considered less significant than the prominent known factors but could still represent a possible cause of bleeding in these patients who do not exhibit any known risk factors for ICH.

The findings also revealed a significant number of cases of ICH in children, particularly neonates, with a prevalence of risk factors that differ from those commonly seen in adults. This necessitates giving due attention to ICH in children in future research to identify the most important existing risk factors and to determine the prognosis and complications associated with ICH in this population.

## 6 | Limitations

There are several potential risk factors for ICH that were not included in this study due to a lack of recorded information in patient records, which do not investigate all possible factors contributing to bleeding. Additionally, the prognosis and mortality rates of patients with ICH were not reported in this study because they were absent from the patient records.

Although this study was conducted in some of the major hospitals in Damascus, which are significant health centers in Syria, gathering information from other provinces could provide a more comprehensive understanding and more accurate data regarding the prevalence of risk factors among patients with ICH.

### Author Contributions

**Mohamad Ala Rashi:** methodology, data curation, investigation, project administration, writing – original draft, writing – review and editing. **Khaled Alkhateeb:** data curation, writing – original draft. **Hamza Altabbaa:** data curation, writing – original draft. **Omar Alnehlawi:** data curation, writing – original draft. **Aman Nakawah:** supervision, writing – review and editing. **Ghassan Hamzeh:** supervision.

### Ethics Statement

The ethical approval was obtained from the Biomedical Research Ethics Committee (BMREC) at Damascus University with ID Number (MD-020624-243).

### Consent

All patients included in the study were thoroughly informed of the authors' intent to access their medical records, and verbal consent was obtained via telephone contact.

### Conflicts of Interest

The authors declare no conflicts of interest.

### Data Availability Statement

The data that support the findings of this study are openly available in Google Drive at https://drive.google.com/drive/folders/1g9ilB3bYIBdSDOVaGeQjQIsv5Si5LeV6.

### Transparency Statement

The lead author Mohamad Ala Rashi affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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