Received: 25 March 2021 / Accepted: 15 June 2021 / Published online: 30 June 2021

DOI 10.34689/SH.2021.23.3.017 UDC 616.12-008.313(581)

## ATRIAL FIBRILLATION PREDICTORS IN PATIENT WITH ACUTE CORONARY SYNDROME IN KABUL (AFGHANISTAN) FROM 2018 TO 2020

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#### **Abstract**

**Aim**: The study was aimed to find out the atrial fibrillation predictors in patient with acute coronary syndrome in Kabul, Afghanistan from 2018 to 2020.

**Methodology**: It was a cross-sectional descriptive study based on purposive sampling conducted in three different hospitals in Kabul. The study included 1416 both male and female patients with known ACS (148 AF) aging over 20 years.

**Results**: The mean age was 59±13 (22-95), the mean systolic BP was 128± 24 (60-210) mmHg, diastolic BP was 82±15 (40-125) mmHg, and mean BMI was 26.1±4.6 (16.1-37.7), CHA2DS2-VASc score was strongly associated with AF (P value < 0.001, 95% CI: 1.36-1.99) and the cases of AF significantly increased with increasing CHA2DS2-VASc score. In addition, mean CHA2DS2-VASC score was different across AF group (2.85 ± 1.64 vs. 2.23±1.23 P value 0.001). AF was more prevalent in hypokalemia (75.10% P value < 0.001) and the mean serum potassium was significantly different across AF group (3.83±0.66 vs. 4.28±0.62 in sinus rhythm). AF prevalence was more in the elevated WBC group (P value 0.001) and there was a strong correlation between AF and WBC (pearson correlation 0.9). Moreover, mean WBC count was different across AF group (10400 ±2900 vs. 9500±3200 in sinus rhythm.

**Conclusion**: Atrial fibrillation is the most common heart rhythm disorder that is strongly and significantly associated with increased CHA2DS2-VASc score, elevated WBC count and low serum potassium level. Patients with these disorders should be closely monitored and serum potassium level should be kept over 3.5 mEq/L. A large cohort study is needed to propose these tests for the screening purpose of atrial fibrillation development in patients with acute coronary syndrome.

Keywords: atrial fibrillation, acute coronary syndrome, AF predictors, Afghanistan.

#### Резюме

## ПРЕДИКТОРЫ ФИБРИЛЛЯЦИИ ПРЕДСЕРДИЙ У ПАЦИЕНТОВ С ОСТРЫМ КОРОНАРНЫМ СИНДРОМОМ В КАБУЛЕ (АФГАНИСТАН) С 2018 ПО 2020 ГОД

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**Цель**. Исследование было направлено на выявление предикторов фибрилляции предсердий у пациента с острым коронарным синдромом в Кабуле, Афганистан с 2018 по 2020 год.

**Методы.** Было проведено перекрестное описательное исследование на основе целенаправленной выборки, проведенной в трех разных больницах г. Кабула. В исследование были включены 1416 пациентов мужского и женского пола с установленным ОКС (148 ФП) в возрасте старше 20 лет.

**Результаты.** Средний возраст составлял 59±13 (22-95) лет, среднее систолическое АД составляло 128± 24 (60-210) мм рт. ст., диастолическое АД составляло 82±15 (40-125) мм рт.ст., а средний ИМТ составлял 26,1±4,6 (16,1-

37,7), Показатель CHA2DS2-VAScдостоверно коррелировал ФП (значение P < 0.001, 95% ДИ: 1,36-1,99), и случаи ФП значительно увеличивались с увеличением показателя CHA2DS2-VASc. Кроме того, средний балл CHA2DS2-VASC был различным в группе с ФП (2,85  $\pm$  1,64 против 2,23 $\pm$ 1,23, значение P 0,001). ФП была более распространена при гипокалиемии (75,10% P < 0.001), а средний уровень калия в сыворотке крови значительно отличался в группе ФП (3,83 $\pm$ 0,66 против 4,28 $\pm$ 0,62 в синусовом ритме). Распространенность ФП была больше в группе с повышенным уровнем WBC (значение P 0,001), и между ФП и WBC была достоверная корреляция (корреляция Пирсона 0,9). Кроме того, среднее количество WBC было различным в группе ФП (10400  $\pm$ 2900 против 9500 $\pm$ 3200 в синусовом ритме.

Заключение. Фибрилляция предсердий является наиболее распространенным нарушением сердечного ритма, которое сильно и значительно связано с повышением показателя CHA2DS2-VASc, повышением количества лейкоцитов и низким уровнем калия в сыворотке крови. Пациенты с этими нарушениями должны находиться под тщательным наблюдением, и уровень калия в сыворотке крови должен быть выше 3,5 мэкв/л. Необходимо большое когортное исследование, чтобы предложить эти тесты для скрининга развития фибрилляции предсердий у пациентов с острым коронарным синдромом.

**Ключевые слова:** фибрилляция предсердий, острый коронарный синдром, предикторы фебрилляции предсердий, Афганистан.

#### Түйіндеме

# 2018 ЖЫЛДАН 2020 ЖЫЛҒА ДЕЙІН АУҒАНСТАННЫҢ КАБУЛ ҚАЛАСЫНДА ЖЕДЕЛ КОРОНАРЛЫҚ СИНДРОМЫ БАР НАУҚАСТА АТРИАЛЬДЫ ФИБРИЛЛЯЦИЯНЫ БОЛЖАУШЫЛАР

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**Мақсаты**. Зерттеу 2018 жылдан 2020 жылға дейін Ауғанстанның Кабул қаласында жедел коронарлық синдромы бар науқаста атриальды фибрилляцияны болжауға бағытталған.

**Әдістеме.** Бұл Кабулдың үш түрлі ауруханаларында жүргізілген мақсатты іріктеуге негізделген кросссипаттамалық зерттеу болды. Зерттеуге 20 жастан асқан 1416 еркек және әйел пациенттері (148 ФП) кірді.

**Нәтижелер.** Орташа жасы  $59\pm13$  (22-95) жыл, орташа систолалық қан қысымы  $128\pm24$  (60-210) мм рт.ст. болды. ст., диастолалық қан қысымы  $82\pm15$  (40-125) мм рт.ст. орташа BMI  $26,1\pm4,6$  (16,1-37,7) болды, CHA2DS2-VASc FP-мен қатты байланысты болды (р < 0,001, 95% di мәні: 1,36-1,99) және FP жағдайлары CHA2DS2-VASc көрсеткішінің жоғарылауымен айтарлықтай өсті. Сонымен қатар, CHA2DS2-VASC орташа балы FP тобында әр түрлі болды ( $2,85\pm1,64$  қарсы  $2,23\pm1,23$ , P мәні 0,001). ФП гипокалиемияда кең таралған (75,10% P < 0,001), ал қан сарысуындағы калийдің орташа деңгейі ФП тобында айтарлықтай ерекшеленді ( $3,83\pm0,66$  қарсы Синус ырғағында  $4,28\pm0,62$ ). FP-нің таралуы WBC деңгейі жоғары топта көбірек болды (р мәні 0,001) және FP мен WBC арасында қатты корреляция болды (Пирсон корреляциясы 0,9). Сонымен қатар, WBC орташа саны FP тобында әр түрлі болды (синус ырғағында  $10400\pm2900$  және  $9500\pm3200$ .

**Қорытынды.** атриальды фибрилляция-бұл жүрек ырғағының ең көп кездесетін бұзылуы, ол CHA2DS2-VASc деңгейінің жоғарылауымен, ақ қан клеткаларының көбеюімен және қан сарысуындағы калийдің төмен деңгейімен байланысты. Бұл бұзылулары бар науқастар мұқият бақылауда болуы керек және қан сарысуындағы калий деңгейі 3,5 мэкв/л-ден жоғары болуы керек.Жедел коронарлық синдромы бар науқастарда атриальды фибрилляцияның дамуын тексеру үшін осы сынақтарды ұсыну үшін үлкен когорттық зерттеу қажет.

Түйінді сөздер: атриальды фибрилляция, жедел коронарлық синдром, ФП предикторлары, Ауғанстан.

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Ibrahimi I., Shinwari N., Sarwari Z., Karibayev K.R., Akhenbekova A.Z. Atrial fibrillation predictors in patient with acute coronary syndrome in Kabul (Afghanistan) from 2018 to 2020 // Nauka i Zdravookhranenie [Science & Healthcare]. 2021, (Vol.23) 3, pp. 146-152. doi 10.34689/SH.2021.23.3.017

*Икрамулла И., Шинвари Н., Сарвари З., Карибаев К.Р., Ахенбекова А.Ж.* Предикторы фибрилляции предсердий у пациентов с острым коронарным синдромом в Кабуле (Афганистан) с 2018 по 2020 год // Наука и Здравоохранение. 2021. 3(T.23). С. 146-152. *doi 10.34689/SH.2021.23.3.017* 

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#### Introduction.

Atrial fibrillation is a common heart rhythm disorder that complicates acute coronary syndrome in about 10-15% casesresulting in deleterious outcomes such as heart failure, thromboembolic events and mortality [1, 2]. Pulmonary veins which have their distinctive architecture and electrical properties, contribute to the reentry and ectopic firing which are the two leading mechanisms of atrial fibrillation initiation such that autopsy examinations revealed the presence of purkinje fibers, transitional and pacemaker cells [3]. Moreover, An appraisal of the data from the healthcare system of the United States showed that the 1year direct cost for a patient with AF was \$20,670 compared to \$11,965 for a patient with a similar co-morbidity profile without AF from 2004 through 2006 in which inpatient services posed the most important cause of the cost difference followed respectively by OPD and emergency department visits [4]. Atrial fibrillation and acute coronary syndrome share almost the same risk factors including advancing age, diabetes mellitus, hypertension, smoking, dyslipidemia, heart failure, obesity, physical inactivity, and alcohol all of which in fact cause electrical and structural remodeling which are counted as necessary substrates for reentry and ectopic firing [5-10]. AF markedly increases mortality in patients suffering from ACS [11], moreover, 17. 9% deaths in women and 14% deaths in men in the year 2010 were from cardiovascular diseases in Afghanistan [12]. CHA2DS2-VASc score was designed as a clinical rule for stroke risk stratification in non-valvular AF and to judge whether treatment with anticoagulant is needed to avoid future stroke episodes due to thromboemblism caused

Besides the advances in the diagnosis and treatment of the comorbid ACS-AF condition over the last two decades, there are not any inexpensive, non-invasive, easy and accessible tests and scores to predict the onset of atrial fibrillation in patient suffering from acute coronary syndrome for a low income country like Afghanistan where most people cannot afford expensive and invasive tests, so we aimed to reveal whether low serum potassium level,

elevated WBC count and increased CHA2DS2-VASc score could really predict or alarm the AF development in ACS patients or not in the local hospitals in Kabul, Afghanistan.

**Methodology.** Design & setting: This is a descriptive cross-sectional study based on purposive sampling including patients from three leading hospitals (Ibne Sina chest hospital, Amiri medical complex and Wazir Akbar Khan hospital) in Kabul from 2018-2020.

Study subjects: The study includes 1416 both male and female ACS patients aging over 20 years of whom 148 patients had atrial fibrillation. Patients with other diagnoses mimicking ACS or causing AF other than ACS such as valvular disease, COPD, thyrotoxicosis, myocarditis, cardiomyopathies, pulmonary embolism and etc. were excluded from the study.

Data collection and Ethics: Data was collected from the medical record files in medical record rooms of the aforementioned hospitals after receiving an official permission from the authorities. Patients' information and variables of interest were collected and entered to the excel database sheet but the patients' identity was intentionally hidden for ethical purpose and serial numbers were used instead.

Data analysis: Data was analyzed in SPSS version 26 using mean ± standard deviation for continuous variables and frequencies & percentages for categorical variables. Logistic regression was run to see the effect of continuous variables on AF and Chi square test was applied to see the difference between categorical variables, furthermore, the difference in medians of continuous variables were analyzed between AF and sinus rhythm using independent samples test. Statistical significance was set at P value less than 0.05.

#### Results

Demographics and baseline characteristics: The study included 1416 known ACS patients (148 AF); 585 of whom were male and 831 were female. Most patients in the study were greater than 60 years of age and 53.3% patients had elevated BMI (52.3%). Most patients came from the Kabul city (55.9%) and low- income families (69.2%). Further patient demographic characteristics are described in table 1.

Table 1.

### **Demographic Characteristics.**

Demographic Characteristic		Frequency	Percentage	
Condor	Male	585	41.3%	
Gender	Female	831	58.7%	
	20-39	88	6.2%	
Age Group	40-59	587	41.5%	
	60 and up	741	52.3%	
	Underweight	15	1.1%	
PMI Croup	Normal weight	646	45.6%	
BMI Group	Overweight	280	19.8%	
	Obese	475	33.5%	
	Poor	981	69.2%	
Income Status	Fair	351	24.8%	
	Good	84	5.9%	
Marital Status	Married	1325	93.6%	
	Unmarried	91	6.4%	
Religion	Islam	1386	97.9%	
	Others	30	2.1%	
Region	Kabul City	792	55.9%	
	Kabul Districts	486	34.3%	
	Other Provinces	138	9.8%	

The mean age was  $59\pm13$  (22-95), the mean systolic BP was  $128\pm24$  (60-210) mmHg, diastolic BP was  $82\pm15$  (40-125) mmHg, height was  $1.7\pm0.08$  (1.5-1.84) m, weight was  $75.5\pm14.8$  (40-110)kg BMI was  $26.1\pm4.6$  (16.1-37.7), CHA2DS2-VASc score was  $2.3\pm1.3$  (0-8), potassium was  $4.2\pm0.64$  (3-7.5) mEq/L, creatinine was  $1.17\pm0.74$  (0.4-5.8) mg/dl, Hb was  $13\pm2$  (6.7-19.6) g/dl and the mean WBC was  $9600\pm3200$  (3700-22900) /µL.

AF predictors: With the increasing CHA2DS2-VASc Score, the prevalence of AF significantly increased

specifically with CHA2DS2-VASc Score of 4 and up i.e. atrial fibrillation prevalence being the least at CHA2DS2-VASc Score 1 (6.9%) and the most at CHA2DS2-VASc Score 8 (100%) in comparison to sinus rhythm (P <0.001, 95% CI 1.36-1.99). For more clarification the prevalence of atrial fibrillation across different CHA2DS2-VASc Score is shown in table 2. In fact, with CHA2DS2-VASc Score of 8 there was no sinus rhythm acute coronary syndrome case and the prevalence of atrial fibrillation was 100% with the mentioned score.

Table 2.

#### CHA2DS2-VASc score & AF.

CHA2DS2- VASc Score	Sinus Rhythm	AF	Total	P value	95%Confidence interval	
					Lower	upper
0	91.2%	8.8%	100%	< 0.001	1.36	1.99
1	93.1%	6.9%	100%			
2	91.1%	8.9%	100%			
3	91.7%	8.3%	100%			
4	84.4%	15.6%	100%			
5	72.9%	27.1%	100%			
6	50.0%	50.0%	100%			
7	0.0%	100%	100%			

For more clear visualization, figure 1 shows the association between AF and CHA2DS2-VASc score.

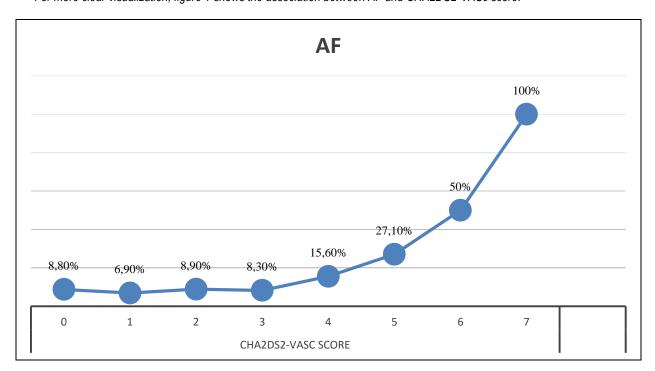


Figure 1 Association between AF & CHA2DS2-VASc score

Figure 1 reveals that with the increasing CHA2DS2-VASc score considerably from 4 and on the prevalence of AF steeps.

The prevalence of AF across serum potassium groups is shown in figure 2.



Figure 2. AF & serum potassium levels.

As shown in figure 2, most AF cases occurred in patient with hypokalemia (75.1% 2P value <0.001) followed by hyperkalemia (13.7%) and normal potassium level (11.2%).

The prevalence of AF increased at higher WBC counts as shown in figure 3.

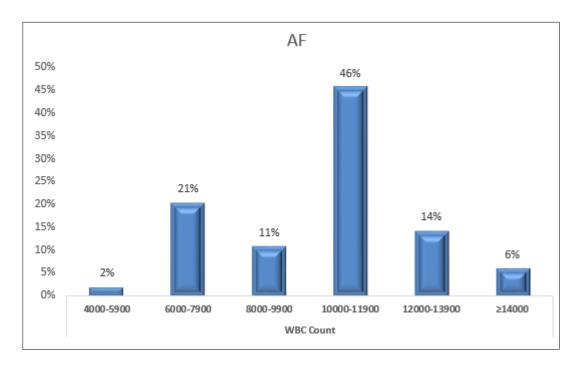


Figure 3. AF across WBC counts.

AF prevalence was higher in WBC count between 10000-11900 (46%) followed respectively by WBC count 6000-7900 (21%), 12000-13900 (14%), 8000-9900 (11%), and 4000-5900 (2%) i.e. AF had strong correlation with WBC count (pearson correlation 0.9, 2P value <0.001).

The means of CHA2DS2-VASc score, serum potassium level and WBC count were different across AF and sinus

rhythm. In fact, mean CHA2DS2-VASc score and WBC count were higher in the atrial fibrillation group compared to sinus rhythm but the mean potassium level was lower in the atrial fibrillation group compared to the sinus rhythm and the differences were statistically significant (P value 0.001) as shown in table 3.

Table 3.

#### Comparison of means between AF & sinus rhythm.

AF predictor	Mean ± SD	Mean± SD	minimum	maximum	P value
	AF group	sinus rhythm			
CHA2DS2-VASc score	2.85±1.64	2.23±1.23	0	8	0.001
Serum potassium	3.83±0.66	4.28±0.62	3	7.5	0.001
WBC count	10400±2900	9500±3200	3700	22900	0.001

#### Discussion

This was the first study conducted in the local hospitals of Kabul city in Afghanistan on the predictors of atrial fibrillation in patients with acute coronary syndrome.

The major finding of the study included the strong and significant association between the three predictors such as CHA2DS2-VASc score, serum potassium level and WBC count with the prevalence or development of atrial fibrillation in patients with underlying acute coronary syndrome disease. As the CHA2DS2-VASc score increased, the prevalence of AF increased accordingly and the difference was significant at P value less than 0.001. Our finding is supported by the finding of Aksoy et al. demonstrating that higher CHA2DS2-VASc score predicted AF in ACS patients [14]. The components of CHA2DS2- VASc Score [15] are associated with elevated inflammatory response in patients [164], and the mechanism and association of inflammation are well known in the development of atrial fibrillation [16].

The reason why serum potassium is lower in patients with myocardial ischemia is that Na–K ATPase pump is activated by adrenergic stimulus in myocardial ischemia resulting in hypokalemia [17]. And serum potassium level was strongly correlated with AF i.e. the prevalence of atrial fibrillation was high in the hypokalemic ACS patients which is consistent with many studies in the literature [18-20].

WBC count was strongly correlated with the AF i.e. AF prevalence was higher in higher counts of WBC and lower in the lower WBC counts; which is in fact, consistent with the finding of Framingham Heart Study and the Atherosclerosis Risk in Community [21-22] and Boyrne et al [23]. Moreover, in a study by Tran et al. high WBC count later in the acute hospital stay is associated with increase in the risk of AF development, and they claim that every 109 cells/L increase in WBC caused about 14% higher risk of AF development. However, it is controversial with the finding of a study conducted in Japan [24]. in fact, his idea is supported by Byrne et al. who found a positive correlation between a raised WBC count and elevated C- reactive protein level [23] which is elevated in inflammatory conditions.

#### Conclusion

Atrial fibrillation is the most common heart rhythm disorder that is strongly and significantly associated with increased CHA2DS2-VASc score, elevated WBC count and low serum potassium level. Patients with these disorders should be closely monitored and serum potassium level should be kept over 3.5 mEq/L. A large cohort study is needed to propose these tests for the screening purpose of atrial fibrillation development in patients with acute coronary syndrome.

#### Limitation

The study has a few limitations, first of which is the design being cross-sectional in which the results may have been affected by confounders. Second, the unavailability of holter monitoring may have caused the under estimation of atrial fibrillation cases and finally the unavailability of the C-reactive protein test through which we could make decision on linking the elevated WBC count with the inflammatory process which is a mechanism of the atrial fibrillation onset.

#### Conflict of interest

The authors declare that they do not have any competing interests.

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