IJC Heart & Vasculature 39 (2022) 100978

Contents lists available at ScienceDirect

IJC Heart & Vasculature

journal homepage: www.sciencedirect.com/journal/ijc-heart-and-vasculature

Before the door: Comparing factors affecting symptom onset to first medical contact for STEMI patients between a high and low-middle income country

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ARTICLE INFO

Keywords:
STEMI
Barriers
Symptom onset
Fist medical contact
Low-middle income

ABSTRACT

Background: Early reperfusion in patients with ST-segment elevation myocardial infarction (STEMI) has been associated with preservation of left ventricular function and decrease in mortality. Symptom onset to first medical contact (FMC) time consumes the majority of total ischemic time, and remains one of the main reasons that patients do not receive timely care. With FMC to reperfusion time being effectively reduced in many parts of the world, the focus is now shifting to reducing symptom onset to FMC times.

Methods: This mixed-methods observational study was designed to elucidate factors affecting symptom onset to FMC time at a regional cardiac center in a low-middle income country (LMIC) and a high-income country (HIC). A review of the Aswan Heart Center and Hamilton General Hospital STEMI registry in Egypt and Canada was conducted, and retrospective semi-structured questionnaires carried out for a convenience sample of 158 patients.

Results: Gender, symptom type and severity were none-modifiable factors found between early and late presenters. Modifiable factors found were actions of bystanders, actions of patients, transportation method and time. Emotional factors also showed differences between the two groups.

Conclusion: While some concepts are generalizable, contextual differences in demographics, risk factors, access and knowledge are identified. These factors can be used to inform tailored knowledge translation strategies to help reduce symptom onset to FMC in both LMIC and HIC.

1. Introduction

Ischemic heart disease has risen 41% since 1990 to become the leading cause of global deaths [1]. This burden is concentrated in low- and middle-income countries (LMIC) where 85% of the world's population now lives [2]. ST-segment elevation myocardial infarction (STEMI) accounts for approximately 25–40% of total myocardial infarction (MI) presentations [3]. Numerous studies have shown the association of early reperfusion in patients with STEMI, particularly within the first 12 h of symptom onset, with increased preservation of left ventricular function and decreased mortality [4,5]. This is reflected in current guidelines, with a recommendation of revascularization (either fibrinolysis or primary percutaneous coronary intervention-PCI) to be delivered as soon as possible and within 12 h of symptoms onset [3].

Total ischemic time involves both (1) symptom onset to first medical contact (FMC) and (2) door-to-balloon (D2B) time [6]. With D2B time effectively optimized in many parts of the world, the focus is now

Abbreviations: AHC, Aswan Heart Center; DM, Diabetes Miletus; EMS, Emergency medical services; FMC, first medical contact; HGH, Hamilton General Hospital; HIC, High-income country; HT, Hypertension; LMIC, low- and middle-income countries; MI, Myocardial infarction; REB, Research ethics board; RSQ, Response to Systems Questionnaire; SD, standard deviation; SO, Symptom onset; STEMI, ST-segment elevation myocardial infarction.

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https://doi.org/10.1016/j.ijcha.2022.100978
Received 15 November 2021; Received in revised form 5 February 2022; Accepted 18 February 2022
Available online 8 March 2022

shifting to reducing symptom onset to FMC. Symptom onset to FMC consumes the majority of total ischemic time, and remains one of the main reasons that patients do not receive timely care [7]. To target this barrier, a better understating of the factors that affect symptom onset to FMC time must be explored. Furthermore, it is suspected that these factors are contextual and do not necessarily apply to a high-income country (HIC) and LMIC alike. This mixed-methods observational study was designed to elucidate the factors affecting symptom onset to FMC from the patients and health system perspective, comparing a newly developed regional cardiac center in a LMIC and a well-established cardiac center in a HIC.

2. Methods

2.1. Setting

Egypt is a LMIC located in north Africa [8], with Aswan being its southernmost governorate. With an area of is 62,726 km^2 the governorate includes both urban and rural communities [9], The Aswan Heart Center (AHC), a tertiary cardiac center established in 2009, provides free cardiac care for the 1.5 million inhabitants in Aswan and the surrounding regions. The sole catheterization laboratory is located at the AHC. In January 2014, the lab's services expanded to include a 24/7 primary PCI program.

The Hamilton General Hospital (HGH) is a tertiary care center located in a large urban community, which covers an area >7000 km^2, and population of over 1.4 million. As one of the busiest cardiac centres in Canada, HGH has a well-established regional STEMI program predominantly providing primary PCI program that has been operating for over 15 years [10].

2.2. Database methodology

A review of the AHC STEMI registry and the HGH STEMI registry was conducted. Clinical data was collected by physicians and catheterization laboratory staff for all STEMI patients as part of an ongoing prospective registry. The data was divided into six main categories: demographics (sex and age), risk factors (hypertension, diabetes and smoking), cardiac history (history of CABG or primary PCI), MI specification (type and location of MI, cardiogenic shock), mortality, and time factors (symptom onset to FMC). FMC was defined as symptom onset to the time that the patient first presented to a medical facility. All patients from the registry who have undergone a primary PCI from January 2015 to February 2016 were included in this study. Patients with a symptom onset to FMC delay of >24 h were excluded as outliers. Research ethics board (REB) approval was obtained (Hamilton REB #2016–1223, Aswan REB #00019142).

2.3. Questionnaire methodology

A modified version of the Response to Systems Questionnaire (RSQ) [11,12] that captures the six domains and basic demographic data was developed and reviewed by a panel of experts from both AHC and McMaster University/Population health Research Institute/Hamilton Health Sciences. The questionnaire was then tested for readability, over the phone, in a sample of 10 patients, and minor changes were made based on responses received. This pilot of 10 patients was not included in the results of the final study. The instrument was translated into Arabic for use at AHC and semi-structured questionnaires were carried out by the health care team retrospectively for a convenience study sample of 80 patients from the HGH STEMI registry, and 78 patients from the AHC STEMI registry. Patients were stratified by early (≤180 mins) and late (>180 mins) presentation to FMC. This timeline was adopted from the ACCF/AHA guidelines for the Management of STEMI (2013), where presentation "very early after symptom onset" is <2 to 3 h [3]. In order to reduce recall bias, the most recently presenting patients in each category (early and late presentation), at each site, were interviewed using consecutive sampling. Following verbal consent, the 10-minute questionnaire was administered over the phone by a health care provider. Non-English or Arabic speakers were excluded. Consecutive patients were contacted a total of three times on separate days, after which they were considered non-responders. The last set of phone interviews was conducted no later than June 2016.

2.4. Data analysis

Time factors were measured overall, as well as for late and early presentation by mean, standard deviation, median, interquartile range, minimum and maximum. Patient characteristics (demographics, risk factors, cardiac history), MI specification, health outcomes, and potential factors affecting time from symptom onset to FMC were described overall and for early and late presenters, and compared between the two groups using standard methods. Categorical variables were described by numbers and percentages, and compared with Chi-Square test. Numerical variables (age) were described by mean, standard deviation, and compared using a *t*-test. Potential factors affecting symptom onset to FMC derived from the questionnaire were described using this same approach. Ordinal variables (e.g. pain intensity, perception questions) were described by numbers and percentages, and compared using a Mantel-Haenszel Chi-Square Test. The modified version of the RSQ, a 7-point Likert scale (range: 10–70) was described using means, standard deviation and compared using a *t*-test. Statistical significance was evaluated at an alpha level of 0.05.

3. Results

3.1. STEMI registry

The Hamilton General Hospital STEMI registry included a total of 715 patients during the study period, none of which were excluded from analysis (Fig. 1). Mean symptom onset to FMC times was 248 min (SD 377.5), median 92 min, with the minimum being 3 min, and maximum 1440 min. Comparatively, the Aswan STEMI database included a total of 585 patients, of which 49 were excluded due to undocumented symptom onset to FMC time, and 10 excluded due to symptom onset to FMC time over 24 h (Fig. 1). Data on the remaining 526 patients was analyzed. Total number of patients with available data (N) for each demographic characteristic differs due to missing values. Mean symptom onset to FMC time was 258 min (SD 267) and median 180 min, with the minimum being 5 min, and maximum 1440 min. Symptom onset to FMC times at HGH were shorter than those seen at the AHC, with a difference in mean delays of 10 min and median difference of 88 min ($P = 0.58$).

Comparative data between the two centers is shown in Table 1. Patients presenting to HGH were older than those presenting at AHC. In both locations, more men than women presented to the centers overall, and at AHC, late presenters had a significantly higher proportion of females (17% versus 26.3%, $P = 0.01$). The majority of patients at HGH had a history of hypertension, were non-smokers and did not have a history of diabetes, with a statistically significant difference between the two sites in all three domains.

There were similar overall proportions of patients with cardiogenic shock at both centers and no significant difference between delay groups. There was a significant difference for in-hospital mortality between the two sites (6.1% for AHC and 3.5% for HGH, $P = 0.032$), with no difference in mortality between delay groups.

3.2. Questionnaire

The questionnaire included 158 patients, with 80 from HGH and 78 from AHC. This was further divided into early and late delay groups, with 40 patients in each category at HGH, 40 patients in the early delay group in AHC and 38 patients in the late delay group at AHC.

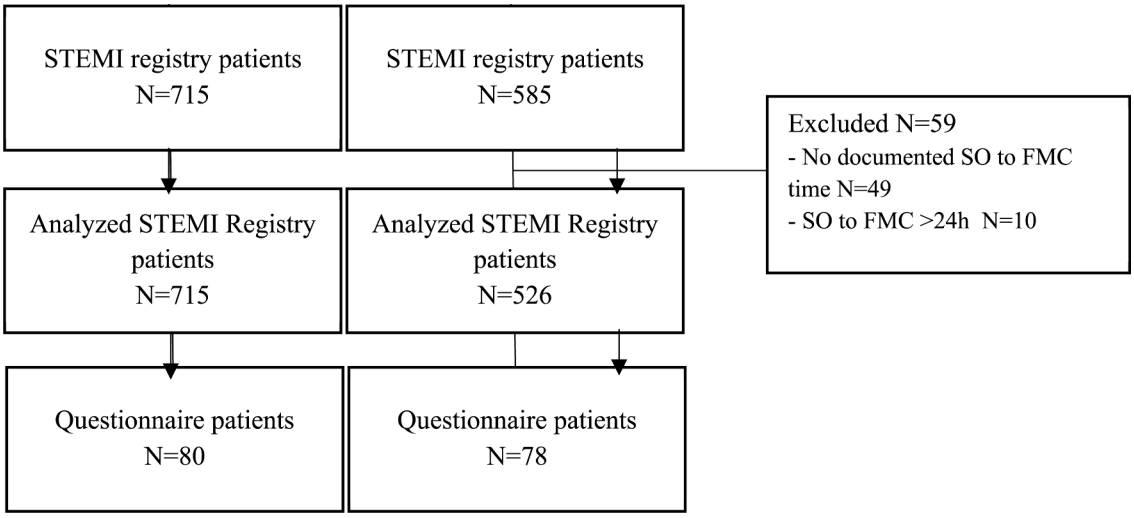

Fig. 1. Study Profile.

Table 1
Baseline characteristics of early and late presenting STEMI patients presenting at the Aswan Heart Center compared to Hamilton General Hospital.

Characteristic	≤180 mins			>180 mins			Overall		
	HGH (N = 508)	AHC (N = 294)	p-value	HGH (N = 207)	AHC (N = 232)	p-value	HGH (N = 715)	AHC (N = 526)	p-value
Age (Mean, SD)	63, 12.3, n = 508	56.6, 11.8, n = 294	<0.001	65, 13.2, n = 207	56.9, 12.3, n = 232	<0.001	63, 12.6, n = 715	56.7, 12.03, 526	<0.001
Gender (Male) (%)	73, n = 508	83, n = 294	0.001	70.5, n = 207	73.7, n = 232	0.458	72.3, n = 715	78.9, n = 526	0.008
DM (%)	19.7, n = 508	39.8, n = 294	<0.001	23.1, n = 207	47.8, n = 232	<0.001	20.7, n = 715	43.3, n = 526	<0.001
HT (%)	51.2, n = 508	39.1, n = 294	0.001	58.5, n = 207	37.9, n = 232	<0.001	53.3, n = 715	38.6, n = 526	<0.001
Smoking (%)	40.4, n = 508	69.3, n = 293	<0.001	42, n = 207	56.8, n = 229	0.002	40.8, n = 715	63.7, n = 522	<0.001
Cardiogenic Shock (%)	15.4, n = 508	11.4, n = 293	0.119	11.6, n = 207	15.9, n = 232	0.188	14.3, n = 715	13.4, n = 522	0.667
In-Hospital Mortality (%)	2.8, n = 508	4.8, n = 272	0.141	5.3, n = 207	7.8, n = 218	0.302	3.5, n = 715	6.1, n = 490	0.0319

3.2.1. Education and employment

The majority of the patients presenting at HGH had completed university education and were retired, while the majority at AHC had not completed a degree and were employed. Overall, most patients at HGH and AHC had no previous cardiac history. There was no significant difference between late and early presenters in these categories.

3.2.2. Symptoms

Symptom onset for the majority of patients occurred at home and with family members present. The majority of patients at both sites experienced chest discomfort. There was a significant difference in symptoms between early and late presenters at AHC More patients experienced light headedness in the late compared to the early group (36.8% compared to 12.5%; P = 0.01). The majority of patients at both sites did not attribute their symptoms to an MI.

Almost all patients at both sites experienced <5 symptoms. The majority of patients at both sites complained of pain intensity of 7–10 (higher score correlating with worse pain) with a significant difference between early and late presenters at AHC (95% vs 71.05% with pain intensity 7–10 respectively; P = 0.005).

3.2.3. Bystander and patient action

There was a significant difference between bystander action between early and late presenters, as well as between sites. At HGH, 62.5% of bystanders called emergency medical services (EMS) in the early group, compared to 25% in the late group (P = 0.0142). Similarly, at AHC, the majority of bystanders in the early group called EMS (74.4%) compared to only 13.6% in the late group (P < 0.001). with more bystanders overall calling EMS compared to HGH. Both sites showed a significant difference in patient actions between early and late presenters. At HGH, patients most frequently first told someone about their symptoms or tried self-treatment/help, compared to AHC where patients called/went to a physician or tried self-treatment/help. At HGH, 23% of patients in the late group pretended nothing was wrong compared to 2.5% of patients in the early group, and no patients called EMS in the late group compared to 7.5% in the early group. Furthermore, 50% of patients in the early group told someone about their symptoms, compared to 32.5% in the late group (P = 0.02). At AHC, in the early group, the majority of patients called/went to a physician (37.5%), while the majority of patients in the late group self -medicated/tried to self-help (39.5%, P = 0.02).

3.2.4. Transportation

The majority of patients at HGH arrived at the hospital via EMS, with almost all patients having a transport time of <20 min. Comparatively, at AHC the majority of patients used a taxi for transport, with almost all patients taking >40 min to reach care, with a significant difference seen between delay groups. In the early group, 12.5% of patients arrived in <20 min, 27.5% in 20–40 min, and 60% in over 40 min. This is comparable to 100% of patients in the late group with a transport time of over 40 min (P = <0.001). A summary of the results comparing HGH and AHC can be found in Table 2.

3.2.5. Knowledge and emotions

In AHC, knowledge of the importance of rapid intervention during an MI was higher in the early group. While early presenters were more likely to feel anxious due to their symptoms, late presenters were more likely to feel embarrassment in seeking help, initially underestimate

Table 2
Responses to the modified Response to Systems Questionnaire at Hamilton General Hospital and the Aswan Heart Center.

Characteristic, %	HGH Overall (N = 80)	AHC Overall (N = 78)	p-value
Education level			
University/ college	58.75	15.4	<0.001
Occupation			
Unemployed	6.25	34.6	
Employed	22.5	47.4	<0.001
Retired	71.25	17.9	
Cardiac History			
Yes	22.5	29.5	0.316
Location of symptom onset			
Home	80.00	87.2	0.224
Bystanders			
None	31.25	5.13	
Family	62.50	80.77	<0.001
Co-worker	2.50	6.41	
Other	3.75	7.69	
Response of Bystander (where applicable)			
Called EMS	43.75	47.44	
Did nothing	10	2.56	0.008
Suggested getting help	10	17.95	
Suggested rest/medication	10	23.08	
Told you not to worry	0	7.41	
Tried to comfort you	0	1.28	
Patient's first response			
Called EMS	3.75	24.36	
Called/went to physician	7.50	37.18	<0.001
Pretended nothing was wrong	12.50	3.85	
Told someone	41.25	2.56	
Self treatment/help	25.00	25.64	
Tried to relax	3.75	6.41	
Symptoms present			
Chest discomfort	75.00	94.87	
Sweat	16.25	38.46	
Nausea	10.00	21.79	
Light headedness	7.50	24.36	<0.001
Shortness of breath	15.00	44.87	
Discomfort to Jaw/arms	31.25	17.95	
Back pain	7.50	11.54	
Vomiting	8.75	42.31	
Number of symptoms			
1	47.50	2.56	
2	28.75	33.33	
3	20.00	33.33	<0.001
4	2.50	20.51	
5+	1.25	10.26	
Pain intensity			
1–3	5.00	0	
4–6	8.75	15.38	0.0186
7–10	57.50	84.61	
Symptom attribution to MI			
Yes	30.0	20.51	0.1703
Transportation Method			
Driven to Hospital	28.75	1.28	
EMS	60.00	8.97	
Public transit	0	11.54	<0.001
Self transport	11.25	1.28	
Taxi	0	76.92	
Transportation Time			
<20 min	91.25	6.41	<0.001
20–40 min	7.50	14.1	
>40 min	1.25	79.49	

their symptoms, delay seeking care due to not wanting to trouble others, and feel in control over their symptoms. In HGH, the early group was more likely to report initially underestimate their symptoms, delaying seeking care due to not wanting to trouble others, wanting to ensure symptoms were those of an MI before seeking care and having feelings of control over their symptoms. Those in the late group were significantly more likely to report feeling anxious due to their symptoms (Table 3).

4. Discussion

In 1950, the first study to explore factors affecting symptom onset to coronary care unit admission took place in Italy, focusing on patient related sociodemographic and clinical factors. Older age, living alone, diabetes, severe pain, MI occurring outside the home with bystanders, ambulance use and distance from hospital were found to be factors significant to delayed presentation to care [13]. Since, majority of research that addresses processes of care in the management of STEMI focuses on high income countries. To our knowledge, this is the first study to explore barriers and facilitators to timely STEMI care in both HIC and LMIC, in order to optimally inform the need for generalized or context specific interventions. Table 4 summarizes the modifiable and none-modifiable barriers found in these regions. Although some factors themselves cannot be modified, interventions can target both categories of barriers.

Symptom onset to FMC delays were seen at both HGH and AHC. Both patient and systemic factors may have contributed to these delays, with difference between the two regional centers given the unique setting and cultural context of each location.

Presentations at both sites differed in terms of their gender and risk factor distribution. Time differences in presentation related to gender has been attributed to the vaguer, non-cardiac symptoms that women tend to experience, compared to the 'classic' symptoms that have been shown to decrease delay times [14]. This may be compounded with the perception of heart attacks as a condition more likely to be experienced by men [15]. At HGH, there were no significant differences in the time of presentation between men and women, however women were more likely to have a longer symptom onset to FMC delay at AHC. It is worth noting that although women experienced a greater delay, the majority of patients presenting in both sites were men, and as such, men should still be included with women in the focus of future interventions. The majority of patients at AHC were smokers, and a significant portion of the presenters had a previous diagnosis of diabetes mellitus. In Hamilton, more than half of patients presenting had a history of hypertension. The risk profile also highlights target groups for these interventions. The overall higher risk profile seen at AHC may also explain the higher mortality seen at this site compared to HGH.

The type and intensity of symptoms were similar between the two sites. Overall, almost all patients at both sites experienced chest pain, yet the majority did not attribute their symptoms to an MI. This brings attention to the potential lack of patient awareness of MI symptoms, and is contrary to research showing that patients experiencing chest pain, tend to have shorter delay times [16]. Although patients experiencing diaphoresis have been shown to present earlier [16], symptoms that are

Table 3
Likert scale responses to the modified Response to Systems Questionnaire in early and late presenters at Hamilton General Hospital and Aswan Heart Center.

System Questionnaire Responses[a]	HGH Presentation Time			AHC Presentation Time		
	≤180 mins (N = 40) Mean (SD)	>180 mins (N = 40) Mean (SD)	p-value	≤180 mins (N = 40) Mean (SD)	>180 mins (N = 38) Mean (SD)	p-value
Knowledge of importance of rapid intervention during an MI	30.25 (27.50)	20.50 (20.99)	0.0786	53.75 (18.21)	46.05 (18.68)	0.0693
Embarrassment to seek help	68.50 (9.49)	65.50 (14.49)	0.2767	17.50 (15.48)	20.79 (11.00)	0.2812
Awareness of symptoms of MI	32.00 (27.19)	34.75 (26.21)	0.6465	33.00 (22.10)	40.53 (18.88)	0.1108
Initially underestimating Symptoms	39.00 (30.03)	13.75 (13.90)	<0.0001	34.50 (23.31)	48.95 (20.11)	0.0045
Delaying seeking care due to not wanting to trouble other	63.00 (18.97)	38.75 (29.37)	<0.0001	17.75 (16.72)	24.74 (11.79)	0.0357
Wanting to ensure symptoms were those of MI before seeking care	57.50 (23.83)	20.25 (20.82)	<0.0001	27.00 (18.97)	25.00 (16.89)	0.6250
Feeling anxious due to symptoms	21.00 (22.74)	38.00 (26.72)	0.0030	67.00 (6.87)	61.58 (12.42)	0.0213
Feeling of control over symptoms	68.50 (9.49)	47.50 (25.89)	<0.0001	28.25 (19.60)	45.14 (11.46)	<0.0001
Feeling comfortable in seeking medical assistance	13.00 (13.24)	10.75 (4.74)	0.3149	67.25 (9.33)	69.74 (1.62)	0.1047

[a] System Questionnaire included a total of 9 questions with each question comprising of a 7-point likert scale (range: 10–70). Higher scale score responses indicated higher agreement to the questionnaire statement.

Table 4
Modifiable and none-modifiable barriers for symptom onset to FMC

Modifiable barriers	None-modifiable barriers
Action of bystander	Gender
Action of patient	Symptom type
Transportation method	Symptom severity
Transportation time	

non-cardiac in origin have been generally linked to longer delays [17]. These nonspecific symptoms may prove harder for patients to interpret and in-turn lead to the undermining of the seriousness of the situation.

The presence of a bystander during symptom onset has been previously shown to reduced pre-hospital delays, although it has also been conversely noted that bystanders tend to initially support patient's decisions to self-medicate and delay seeking medical care [15] highlighting that it is the healthcare seeking actions by bystanders that affect delay times. In both sites, the majority of bystanders in the early group called EMS with the action taken by bystanders showing a link to timely presentation. These factors stress the importance of including patients' families in education programs, along with the general public, and takes into account the inclusion of family in health care decisions found in some cultures [18].

Another important contribution to delay is the time taken to reach FMC after an individual has made the decision to seek care. It has been previously shown that patients presenting via EMS have a shorter delay to care [7,19,20]. The majority of patients at HGH either arrived by EMS or were driven to the hospital, compared to AHC where taxi and public transport were the most frequently used transportation methods. At HGH, almost all patients had a transport time <20 min compared to AHC, where transport time took >40 min for the majority of patients, in both early and late groups. Given the large region serviced by AHC, this may be attributed to long distances to a hospital, or due to self-transportation. The lack of EMS use at AHC is likely secondary to limitations in the health care infrastructure of the region. This is highlighted by the discrepancy in the number of people who contacted EMS, compared to the number of patients that used the service to reach the hospital. It can be hypothesized that EMS cannot be successfully, or that they cannot provide their service in a timely manner, leading patients to utilize alternative methods of transportation.

The COVID-19 pandemic has presented an additional hurdle for access to care for STEMI patients. A 20% decrease in STEMI hospitalizations has been noted in the literature, with an increase in cases of out-of-hospital cardiac arrest. This has been linked to lower hospital bed availability with a system that is overwhelmed, with speculation about logistic hurdles such as ambulance overload. Interestingly, fear of infection or stay-at-home orders as a barrier to care were found to influence STEMI hospitalization [21].

This study has some limitations. The survey used for this study was not specifically validated, but rather a modified version of a widely used questionnaire. Furthermore, due to the retrospective nature of the data collection for the questionnaire, there may have been recall bias, especially as patients were asked about a particularly stressful event. However, the database was used to supplement the information provided by the patients and only larger themes were drawn from the survey. Future studies can consider carrying out these surveys within 24 h of presentation to further reduce recall bias. Finally, it is also recognized that this study was conducted at specific locations, and this must be kept in mind before generalizing these results to all HIC and LMIC.

5. Future direction and conclusion

This study identified barriers to timely STEMI care in a HIC and LMIC, showing similarities and differences between the two locations. It is important to note these similarities and differences can also exist within each country. Canada is diverse in its population, and accessibility of care, making some results found in LMIC potentially generalizable to parts of the country [22]. These factors can be used to inform knowledge translation strategies to help reduce symptom onset to FMC in both LMIC and HIC.

Declaration of Competing Interest

The authors report no relationships that could be construed as a conflict of interest.

Acknowledgements

Mohamed Elkhateb, Dr. Ahmad Samir, and Renu Syal for assistance in the collection of the data necessary for this study.

Funding sources

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors

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