

## Regional variations in Acute Coronary Syndrome- Insights from Registries

M Maksumul Haq<sup>1</sup>, Saidur Rahman Khan<sup>2</sup>

Cardiovascular diseases (CVD) are the leading causes of morbidity and mortality among adults in the industrialized world. With improved health care and preventive strategy an epidemiological transition in disease pattern is observed in developing countries with infectious diseases declining steadily and chronic disease increasing rapidly.<sup>1</sup>

Among CVDs, acute coronary syndrome (ACS) & coronary artery disease account for approximately 7 million deaths each year.<sup>2,3</sup> ACS, comprising of ST Elevation Myocardial Infarction (STEMI), Non-ST segment Myocardial Infarction (NSTEMI) and Unstable Angina (UA) is a major acute cardiac cause of morbidity and mortality. Management strategy of ACS include Aspirin with P2Y12 inhibitor drugs (Clopidogrel, Prasugrel or Ticagrelor), b-Blocker, ACE Inhibitor, Statin and low molecular weight heparin (LMWH). Early coronary angiogram and angioplasty is recommended for high risk ACS patients. Thrombolytics like Streptokinase (STK) and Tissue Plasminogen Activator (tPA) or primary percutaneous coronary intervention (pPCI) are principal modality of treatment of STEMI cases if patients report within a stipulated time frame. pPCI has a definite advantage over thrombolytic in reducing morbidity and mortality.

Advances in treatment of ACS are made by understanding of its pathophysiology, better

therapeutic interventions and new drugs. Guidelines for treatment are based on both randomized (RCT) and non-randomized clinical trials on selected population. However registries of ACS in different parts of the world are real-life, population-based data. There are variations in the pattern of ACS in different parts of the globe. So are in the treatment modalities. The Asia-Pacific Real world evIdenCe on Outcome and Treatment of ACS (APRICOT)<sup>4</sup> project by reviewing current published and unpublished registry data showed striking heterogeneity in the use of invasive procedures, pharmacologic practice and clinical outcomes across different regions. This heterogeneity was greater in Asia than in Western Europe or the United States.<sup>4</sup> Chinese and Indians showed significantly lower risk of in-hospital mortality compared to Malays with ACS.<sup>5</sup>

The important registries on ACS done worldwide are GRACE (Global Registry of Acute Coronary Events) registry<sup>6</sup> done over several continents, ACTION Registry<sup>7</sup> in USA, ACCESS in 19 countries of Middle East, Latin America & North Africa, Euro Heart Surveys I / II/ III,<sup>8,9</sup> in 47 countries of Europe & Mediterranean basin of Europe, MANTRA registry in Italy;<sup>10</sup> CPACS<sup>11</sup> in China, Kerala ACS Registry,<sup>12</sup> OASIS-2<sup>13</sup> & CREATE<sup>14</sup> in India, CONCORDANCE<sup>15</sup> in Australia, PACIFIC<sup>16</sup> in Japan and GULF RACE<sup>17</sup> & SPACE<sup>18</sup> in middle east.

### Authors' Information:

<sup>1</sup>**M Maksumul Haq**, MBBS (DMC), FCPS (BD), FACC (USA), FRCP (Edin), Clinical & Interventional Cardiologist, Professor & Head of the Department, Department of Cardiology, Ibrahim Cardiac Hospital & Research Institute, Shahbag, Dhaka-1000

<sup>2</sup>**Saidur Rahman Khan**, MBBS (DMC), MD. Ph.D (Card), FACC (USA), Fellow Interventional Cardiology, Associate professor & Consultant Interventional Cardiology, Ibrahim Cardiac Hospital & Research Institute, Shahbag, Dhaka-1000

**Correspondence:** M Maksumul Haq, MBBS (DMC), FCPS (BD), FACC (USA), FRCP (Edin), Clinical & Interventional Cardiologist, Professor & Head of the Department, Department of Cardiology, Ibrahim Cardiac Hospital & Research Institute, Shahbag, Dhaka-1000. E-mail: maksumul@hotmail.com

GRACE studied 43,810 patients from 1999-2005 in 14 countries (USA, Europe, Argentina, Brazil, Canada, Australia, NZ) excluding Africa and Asia showed large difference in treatment practice depending on hospital type and geographic location.<sup>4</sup> Statin use was lower in GRACE of Argentina-Brazil (26%) compared to GRACE USA (53%) and even lower compared to study of Euroheart III (90%). About 10-15 years back when GRACE registry was done thrombolytic were used in 47% and 18% of patients who received pPCI. In this registry it is seen that about 80% of hospitals of Europe and US had catheterization laboratory facility, however in Australia and New Zealand it was around 60% meaning that availability of immediate coronary angiogram and angioplasty procedures if required are not similar in different geographic regions.

ACCESS<sup>19</sup> registry was a prospective, observational, multinational registry comprised of 9,732 number of patients hospitalized for an ACS (Jan 2007 - Jan 2008). Patients were enrolled at 134 sites in 19 countries including Argentina, Brazil, Colombia, Dominican Republic, Ecuador, Guatemala, Mexico, Venezuela, Egypt, Iran, Jordan, Kuwait, Lebanon, Saudi Arabia, United Arab Emirates, Algeria, Morocco, Tunisia and South Africa. In this registry STEMI was 45%, NSTEMI was 24% and UA was 28%. Aspirin, Thienopyridine, Statin, b-blocker and ACE Inhibitor use were 90, 76, 89, 76 and 64% respectively. For STEMI pPCI was used in 26% cases and fibrinolytics in 39% cases. Low molecular weight heparin was used in 58% and coronary angiogram was done in 58% cases. Mortality from STEMI at one year was highest in Latin America (9.9%) followed by North Africa (8.3%), South Africa (6.7%) and Middle East (6.6%).

The largest ACS registry from Kerala, South India on 25,748 patients showed ST segment elevation myocardial infarction (STEMI) to be the most common (37%) followed by non-STEMI (31%), unstable angina (32%).<sup>20</sup> Another study done on 20,468 patients from 89 centers from 10 regions and 50 cities in India showed STEMI more (60.6%) than other forms of ACS which

was unlike in developed countries.<sup>14</sup> In a study done in Pakistan,<sup>21</sup> ACS pattern differed - unstable angina was 43%, STEMI was 40.5% and NSTEMI 16.5%.

Evidence and guideline based management of ACS in developed countries has reduced the ACS related mortality by about 25% over the last decade.<sup>22</sup> However registry data from Asia-Pacific region (other than Australia and New Zealand) shows that ACS related mortality remains high both at hospitalization and one-year post discharge.

Reports from developed countries<sup>23</sup> including the European Heart Survey showed that STEMI incidence was higher in developing nations compared to NSTEMI. The European Network for Acute Coronary Treatment (ENACT)<sup>24</sup> study done over 29 countries across Europe found that UA is a more frequent cause of hospitalization than STEMI & NSTEMI combined (ratio 1.2:1). Management guidelines for ACS are published and updated by different societies; however there is gap between recommendations and practice.<sup>25,26</sup> Management strategy for ACS patients between countries differs due to a variety of reasons including availability of resources, skilled manpower, medical practice pattern and medical insurances.<sup>27</sup> The difference in presentation of ACS and its management also leads to different clinical outcome in these groups of patients as is evident by different registries.

STEMI patients were high in Euroheart III (61%) followed by, 45% in ACCESS, 45% in SPACE registry of middle east, 37% in Kerala registry and 34% in GRACE. Mortality from STEMI was 7% in GRACE, 8.4% in ACCESS, 3.9% in Euroheart III and 8.2% in Kerala Registry.

Following American Heart Association/American College of Cardiology practice guidelines had a positive impact on morbidity and mortality in USA as was shown in National Registry of Myocardial Infarction from 1990 to 2006.<sup>28</sup> Cardiovascular disease is declining in some industrialized countries due to newer technologies & treatment and quality surveillance.

Registries of patients presenting with ACS give us an opportunity to determine whether the cardiac hospitals and in a larger perspective the whole country is practicing guidelines as recommended by international societies. This information can be utilized to determine the risk profile and characteristics of patients experiencing ACS according to the countries they inhabit and to formulate their own guideline based on the availability of resources. It is expected that registries will help in developing formulate a national policy regarding management of ACS based on local resources. This will ultimately have a role for a favorable outcome in our ACS patients. Nationwide comprehensive registry on ACS patients is obviously an important step to evaluate our limitations and possibilities of improving the outcome of ACS patients. We can develop a better treatment strategy according to our present resources and also can make plan for coordinated future steps to make guideline oriented treatment available at our door step.

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