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ORIGINAL ARTICLE

FREQUENCY, DISTRIBUTION AND DETERMINANTS OF DIABETES MELLITUS IN ADULT ACUTE CORONARY SYNDROME POPULATION OF D.I.KHAN DIVISION, PAKISTAN

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ABSTRACT

Background: Global Health Estimates 2015 has shown IHD as second leading global cause of death and 3rd leading global cause for DALYs for 2015. The objectives of this study were to determine frequency, distribution and determinants of DM in adult acute coronary syndrome (ACS) population of D.I.Khan Division, Pakistan.

Materials & Methods: This cross-sectional study was conducted in Departments of Ophthalmology & Community Medicine, Gomal Medical College, D.I.Khan, from February 1, 2017 to April 30, 2017. 331 cases were selected with margin of error 4.511%, 90%CL and 25% prevalence of DM in 73,438 adults assumed to have IHD. All indoor adult patients of ACS were eligible. Sex, age groups, and residence and presence of DM were variables. Frequency and distribution were analyzed by count and percentage. Hypotheses for distribution were substantiated by chi-square goodness-of-fit and of association by chi-square test of association.

Results: Out of 331 patients with ACS, 225 (68.0%) were men and 106 (32.0%) women, 221 (66.8%) ≤60 years and 110 (33.2%) >60 years, and 210 (63.4%) urban and 121 (35.6%) rural. Frequency of DM was 79/331 (23.87%). Out of 79 patients with DM, men were 44 (13.29%), women 35 (10.57%), age group ≤60 years 57 (17.22%), >60 years 22 (6.65%), urban 53 (16.01%) and rural 60 (7.85%). Our prevalence of DM was lower than expected (p=.00214), our distribution by sex was similar to expected (p=.4993) while our distribution for age groups (p=.01209) and residence (p=.00005) were not similar to expected. Presence of DM was associated to sex (p=.011) but not to age groups (p=.0304) and residence (p=.5241).

Conclusion: Prevalence of DM in adult ACS population of D.I.Khan Division, Pakistan was found lower than expected. The prevalence was more in men than women, more in younger age group (≤60 years) than older age group (>60 years) and more in urban than rural population. Our prevalence of DM was lower than expected, our distribution by sex was similar to expected while our distribution for age groups and residence were not similar to expected. The presence of DM was associated to sex but not to age groups and residence.

KEY WORDS: Acute Coronary Syndrome; Myocardial Infarction; Unstable Angina; Diabetes Mellitus; Adult; Global Health; Pakistan; Urban Population; Rural Population; Chi-square Test.

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1. INTRODUCTION

1.1 Background: Our population of interest includes patients with acute coronary syndrome (ACS). Our disease/ variable of interest is presence of diabetes mellitus (DM) in this population. We will first present burden of ischemic heart disease (IHD) in general population, then of DM in general population and then of DM in IHD population. Here we are presenting the burden of the two diseases from WHO website in terms of mortality (deaths)[1] and disabilities (DALYs[2];

Table 1.1.1: WHO Global, EMR & Pakistan data for deaths for ischemic heart disease and diabetes mellitus for years 2015 and 2000.

Area and Year	Population	Total Deaths All causes	DEATHS IHD			DEATHS DM		
			IHD Deaths	% of all deaths	Leading Cause	DM Deaths	% of all deaths	Leading Cause
Global 2015	7,344,362,000	56,441,319	8,756,006	15.5%	1st	1,586,530	2.8%	6th
Global 2000	6,122,410,000	52,134,566	6,882,843	13.2%	1st	957,694	1.8%	12th
EMR 2015	643,784,000	4,023,088	753,000	18.7%	1st	132,000	3.3%	5th
EMR 2000	467,911,000	3,400,392	522,461	15.4%	1st	74,667	2.2%	11th
Pakistan 2015	188,925,000	1,370,800	265,100			43,100		
Pakistan 2000	138,250,000	1,203,200	169,000			20,200		

Table 1.1.2: WHO Global, EMR & Pakistan data for DALYs for ischemic heart disease and diabetes mellitus for years 2015 and 2000.

Area and Year	Population	Total DALYs All causes	DALYs IHD			DALYs DM		
			ACS DALYs	% of Total DALYs	Leading Cause	DM DALYs	% of Total DALYs	Leading Cause
Global 2015	7,344,362,000	2,668,295,338	192,055,503	7.2%	1st	70,667,217	2.6%	8th
Global 2000	6,122,410,000	2,805,625,771	153,892,480	5.5%	3rd	44,896,218	1.6%	16th
EMR 2015	643,784,000	245,997,996	18,145,120	7.4%	1st	6,899,545	2.8%	10th
EMR 2000	467,911,000	226,450,727	13,188,031	5.8%	5th	3,875,452	1.7%	13th
Pakistan 2015	188,925,000	87,503,400	6,178,100			1,867,700		
Pakistan 2000	138,250,000	83,199,300	4,062,900			947,300		

Disability-adjusted life years) globally, regionally (for EMR; Eastern Mediterranean Region) and then nationally for Pakistan, both for 2015 and 2000. Here are complex counts, so these are presented in tables, rather text.

Table 1.1.1 shows data/ counts for deaths and Table 1.1.2 for DALYs, each for the three said geographical areas and both for the year 2015 and year 2000. Going in descending order, the counts are decreasing/ converging, the other way, the counts are increasing/ diverging for each disease, hence showing the trend of the diseases.

Atherosclerotic cardiovascular disease (ACD) is a leading cause of mortality in the developed as well as developing communities worldwide. Although age-adjusted ACD mortality has decreased globally, the absolute number of ACD deaths is increasing due to the population growth and aging, as well as important lifestyle and food-system changes.[3]

The global burden of IHD increased by 29 million DALYs between 1990 and 2010. By 2013, IHD was the leading causes of DALYs. The majority of IHD burden in 2010 affected middle-income regions, where younger adults were more likely to develop IHD in regions such as South Asia and North Africa/ Middle East. Age-standardized IHD DALYs increased in a number of countries in the Eastern Europe/ Central Asia region. The majority of IHD burden affected middle-income regions.[4]

The trend in mortality from IHD was sought from 2004 to 2009 in sample of 73 million people; 6% of all the Chinese population. It showed increasing trend in mortality due to IHD in China versus decreasing mortality trend in other countries. This is thought to be largely by increasing IHD mortality in rural areas and people over 80 years old.[5]

Cardiovascular diseases (CVDs) are the number 1 cause of death globally, taking an estimated 17.9 million lives in year 2016; 31% of all global deaths. CVDs are a group of disorders of the heart and blood vessels and include coronary heart disease, cerebrovascular disease, rheumatic heart disease and other conditions. Out of 17 million premature deaths (under the age of 70) due to non-communicable diseases in 2015, 37% were due to CVDs.[6]

Abbas, et al.[7] had population study published in 2009, involving 2000 persons of >20 years of age from Islamabad capital area of Pakistan and found the prevalence of documented IHD as 6.25% (125/2000).

Type 2 diabetes accounts for more than 90% of patients with diabetes, with 415 million people with diabetes worldwide, with an estimated 193 million people having undiagnosed diabetes. The incidence and prevalence of the disease continues to rise globally.[8]

A household survey from North Indian state of Punjab, India, by Tripathy, et al.[9] conducted in 2013-14, showed the overall prevalence of DM as 8.3% (95%CI 7.3-9.4%) in a sample of 2,465 adults, whereas prevalence of pre-diabetes was 6.3% (95%CI 5.4-7.3%).

A systematic review by Meo, et al.[10] in 2015, including 18 original articles, showed the overall prevalence of type 2 diabetes mellitus in Pakistan as 11.77%.

As a part of first National Diabetes Survey of Pakistan (1st NDSP), conducted between 1994 and 1998 by Shera, et al.,[11] the results for the rural town of Shikarpur, Sindh, Pakistan were published in 1995. A sample of 967 adults >25 years of age was selected, including 387 (40%) men and 580 (60%) women. The prevalence of DM (both known & new cases) was 13.55% (131*100/967), IGT (impaired glucose tolerance) 11.89% (115*100/967) and of NGT (normal glucose tolerance) 74.56% (721*100/967), totaling to 100% (967). The distribution of 13.55% positive cases of DM by sex showed the prevalence in men as 6.52% (63*100/967) and in women as 7.03% (68*100/967), totaling to 13.55% (131/967).

As a part of first National Diabetes Survey of Pakistan (1st NDSP), conducted between 1994 and 1998 by Shera, et al.,[12] the results for the province of NWFP, Pakistan were published in 1999. A sample of 1,035 adults >25 years of age was selected, including 207 (20%) men and 828 (80%) women. The prevalence of DM (both known & new cases) was 18.17% (188*100/1,035), IGT was 9.37% (97*100/1,035) and of NGT was 72.46% (750*100/1,035), totaling to 100% (1,035). The distribution of 18.17% positive cases of DM by sex showed the prevalence in men as 3.00% (31*100/1,035) and in women as 15.17% (157*100/1,035), totaling to 18.17% (188/1,035).

As a part of first National Diabetes Survey of Pakistan (1st NDSP), conducted between 1994 and 1998 by Shera, et al.,[13] the results for the urban and rural areas of Baluchistan Province, Pakistan were published in 1999. A sample of 1,404 adults >25 years of age was selected, including 435 (31%) men and 969 (69%) women and 834 (59.4%) urban and 570 (40.6%) rural. The prevalence of DM (both known & new cases) was 9.05% (127*100/1,404), IGT 11.61% (163*100/1,404) and NGT 79.34% (1,114*100/1,404), totaling to 100% (1,404). The distribution of 9.05% positive cases of DM by sex showed the prevalence in men as 3.35% (47*100/1,404) and in women as 5.70% (80*100/1,404), totaling to 9.05% (127/1,404). The distribution of positive cases of DM by residence showed the prevalence in urban as 6.41% (90*100/1,404) and in rural as 2.64% (37*100/1,404), totaling to 9.05% (127/1,404).

As a part of first National Diabetes Survey of Pakistan (1st NDSP), conducted between 1994 and 1998, the prevalence of DM was determined by performing a cross-sectional survey conducted in all the four provinces of Pakistan. The results were published independently for each of the four provinces earlier under the title of 'The Pakistan National Diabetes Survey'. Here in this cited study by Shera, et al.,[14] the results were amalgamated to achieve a total figure for the country and published in 2007. A sample of 5,433 adults over 25 years of age was selected, including 1,893 (34.84%) men and 3540 (65.16%) women, and 1982 (36.48%) urban and 3451 (63.52%) rural. The prevalence of DM (both known & new cases) was 8.74% (475*100/5,433), IGT 10.20% (554*100/5,433) and NGT 81.06% (4,404*100/5,433), totaling to 100% (5,433). The distribution of 8.74% positive cases of DM by sex showed the prevalence in men as 3.24% (176*100/5,433) and in women as 5.50% (299*100/5,433), totaling to 8.74% (475/5,433). The distribution of 8.74% positive cases of DM by residence showed the prevalence in urban as 3.86% (210*100/5,433) and in rural as 4.88% (265*100/5,433), totaling to 8.74% (475/5,433).

As a part of first National Diabetes Survey of Pakistan (1st NDSP), conducted between 1994 and 1998 by Shera, et al.,[15] the results for the province of Punjab, Pakistan were published in 2010. A sample of 1,852 adults >25 years of age was selected, including 815 (44%) men and 1,037 (56%) women. The prevalence of DM (both known & new cases) was 10.85% (201*100/1,852), IGT 7.35% (136*100/1,852) and NGT 81.80% (1515*100/18,52), totaling to 100% (1,852). The distribution of 10.85% positive cases of DM by sex showed the prevalence in men as 5.34% (99*100/1852) and in women as 5.51% (102*100/1852), totaling to 10.85% (201/1,852).

We wanted to include the findings of the second National Diabetes Survey of Pakistan (NDSP), 2016-2017 by Basit, et al.,[16] in our introduction and discussion. The authors have included counts for sample and sub-samples sizes but not for frequency and distribution of DM by socio-demographic variables. Only percentages (95% CI) are shown for provinces and area (urban/ rural). How 'Count' a basic epidemiologic measurement tool can be ignored in any epidemiologic survey? We required expected counts from this survey for comparison to our observed counts in chi-square goodness-of-fit test but this survey is not in a comparable format.

Yar, et al.[17] from Rahim Yar Khan, Pakistan in a study published in 2009, selected 650 adults >20 years old, including 517 (79.54%) men and 133 (20.46%) women, and 629 (96.77%) in age group up to 60 years and 21 (3.23%) in age group >60 years. The prevalence of DM (both known & new cases) was 19.38% (126*100/650), IGT was 18.92% (123*100/650) and of no diabetes was 61.70% (401*100/650), totaling to 100% (650). The distribution of 19.38% positive cases of DM by sex showed the prevalence in men as 13.54% (88*100/650) and in women as 5.84% (38*100/650), totaling to 19.38% (126/650).

Aamir, et al.[18] conducted a Pakistan-wide community-based survey for the prevalence of type 2 diabetes from April 2017 to November 2017. They included 18,856 adults >19 years of age and used HbA1c as the screening test. The sample included 10,100 (53.56%) men and 8,756 (46.44%) women, 16,294 (86.41%) in age group up to 60 years and 2,562 (13.59%) in age group >60 years, and 12,262 (65.03%) urban and 6,594 (34.97%) rural.

The prevalence of DM (both known & new cases) was 16.98% (95% CI 16.44-17.51) (3201*100/18,856), prediabetes 10.91% (2057*100/18,856) and of no diabetes 72.11% (13,598*100/18,856), totaling to 100% (18,856).

The distribution of 16.98% positive cases of DM by sex showed the prevalence of 8.69% (1638*100/18,856) in men and 8.29% (1563*100/18,856) in women, totaling to 16.98% (3201/18,856).

The distribution of 16.98% (3201/18,856) positive cases of DM by age groups showed the prevalence of 13.54% (2,553*100/18,856) in age group up to 60 years and 3.38% (638*100/18,856) in age group >60 years, totaling to 16.92% (3191/18,856).

The distribution of 16.98% (3201/18,856) positive cases of DM by residence showed 10.24% (1932*100/18,856) in urban and 6.68% (1259*100/18,856) in rural, totaling to 16.92% (3191/18,856).

Ahmad et al.[19] from Abbottabad, Pakistan for the period from October, 2009 to April, 2010, studied 250 acute coronary syndrome (ACS) patients above 25 years age, including 161 (64.4%) men and 89 (34.6%) women. The overall frequency of diabetes in ACS was 31.6% (79*100/250). The distribution of 31.6% positive cases of DM in ACS showed 16.4% (41*100/250) men and 15.2% (38*100/250) women.

Hussain, et al.[20] from Bahawalpur, Pakistan during June 2009-December 2011, studied 605 adult cases of IHD. The frequency of DM in IHD was 36.85% (223*100/605). The distribution of 36.85% positive cases of DM in IHD was 16.69% (101*100/605) in men and 20.16% (122*100/605) in women and 21.65% (131*100/605) in age group up to 60 years and 15.20% (92*100/605) in age group >60 years. Here two group of <40 & 41-60 years were combined for comparison to our one group of up to 60 years.

Note: Aaamir, et al.[18], have shown count for men as 10,116 in text in results. It is correctly given as 10,100 in their Table 1. The sum of counts for five age groups and two area groups of DM positive cases is shown as 3191 in their Table 1 instead of 3201; hence its % is given as 16.92 and the same is distributed by us by age groups and area instead of correct 16.98%.

Further Aaamir, et al.[18], have shown overall frequency of DM as 16.98%, prediabetes as 10.91% and no diabetes as 72.11%, all three combined are totaling to 100%. When 16.98% DM positive cases are distributed by sex, it is shown as 51.17% for men and 48.83% for women, totaling to 100%. It shows that 100% of the sample and the population from where they have drawn this sample are all having DM, and all having prediabetes and all having no diabetes. This story is same for all other surveys cited by us in this article and in many more articles on this title and many more titles in local, national, regional and global literature.

Re-visit our statement given above as "The distribution of 16.98% positive cases of DM by sex showed the prevalence of 8.69% (1638*100/18,856) in men and 8.29% (1563*100/18,856) in women, totaling to 16.98% (3201/18,856)".

All respective stake holders; researchers, publishers, universities, associations, organizations, institutions, countries, including Pakistan Medical & Dental Council, Higher Education Commission, Pakistan, Centers for Disease Control and Prevention, USA, and WHO are requested to re-visit the relevant findings/ results/ conclusions/ recommendations and decisions based on such analysis.

As our analysis of data is different from the many surveys cited above, so we have given detailed calculations for verification of our results for these cited studies.

1.2 Research Problems, Knowledge Gaps & Research Questions:

We don't know the frequency, distribution by sex, age groups and residence, and determinants (association to sex, age groups and residence) of DM in ACS population of D.I.Khan Division, Pakistan. This unawareness of seven pieces of information are our seven Research Problems. Relevant research documents regarding our specified population could not be retrieved through online search through different search engines and databases for these seven problems. These are our seven Knowledge Gaps.

What would be the frequency, distribution by sex, age groups and residence, and determinants (association to sex, age groups and residence) of DM in ACS population of D.I.Khan Division, Pakistan, would be our seven Research Questions.

We have formulated seven Research Hypotheses. These are probable answers to these seven questions derived from the results for many other similar population studies. We would collect relevant data from our population, analyze and interpret it to see if our observed answers match our probable answers or otherwise? These all eight steps constitute "Marwat's Logical Trajectory of Research Process", used in many research papers.[21,22]

1.3 Research Objectives (ROs):

RO1: To determine the frequency of DM in adult ACS population of D.I.Khan Division, Pakistan.

RO2-RO4: To determine the distribution of DM by

sex, age groups and residence in adult ACS population of D.I.Khan Division, Pakistan.

RO5-RO7: To determine the association of DM to sex, age groups and residence in adult ACS population of D.I.Khan Division, Pakistan.

1.4 Research (Null) Hypotheses:

$H_0$1: There is no statistically significant difference between the observed and expected frequency of DM in adult ACS population of D.I.Khan Division, Pakistan.

$H_0$2: There is no statistically significant difference between the observed and expected distribution of DM by sex in adult ACS population of D.I.Khan Division, Pakistan.

$H_0$3: There is no statistically significant difference between the observed and expected distribution of DM by age groups in adult ACS population of D.I.Khan Division, Pakistan.

$H_0$4: There is no statistically significant difference between the observed and expected distribution of DM by residence in adult ACS population of D.I.Khan Division, Pakistan.

$H_0$5: The presence of DM is not associated to sex in adult ACS population of D.I.Khan Division, Pakistan.

$H_0$6: The presence of DM is not associated to age groups in adult ACS population of D.I.Khan Division, Pakistan.

$H_0$7: The presence of DM is not associated to residence in adult ACS population of D.I.Khan Division, Pakistan.

1.5 Operational definitions

Acute Coronary Syndrome: For the purpose of this study, ACS included ST elevation myocardial infarction (MI), non-ST elevation MI and unstable angina.

Diagnostic Criteria for Diabetes: A person is labeled as having diabetes mellitus if he has history of diabetes mellitus and/ or on anti-diabetic medications or symptoms of diabetes mellitus plus one of the following:

1. Fasting plasma glucose of ≥ 126 mg/dL
2. Plasma glucose of ≥ 200 mg/dL in random sample or two hours after 75 gm oral glucose load
3. HbA1c ≥ 6.5%

If the patient is asymptomatic, the above criteria apply but there should be two abnormal tests out of four above from the same or different samples. In case of one abnormal test, it should be repeated on subsequent day. In case the test is normal, the person is non-diabetic; otherwise he is diabetic. In patients with no history of DM, HbA1c will be checked on admission to exclude stress hyperglycemia.[23]

Adult: As defined by WHO "an adult is a person older than 19 years of age unless national law defines a person as being an adult at an earlier age".[24]

2. MATERIALS AND METHODS

2.1 Design, Settings & Duration: This cross-sectional study was conducted in the Departments of Ophthalmology & Community Medicine, Gomal Medical College, D.I.Khan, Pakistan from February 01, 2017 to April 30, 2017. All the three major components of epidemiological investigation were included i.e. frequency, distribution and determinants of a disease. All files of indoor patients of CCU of DHQ Teaching Hospital, D.I.Khan for the period from January 1, 2016 to December 31, 2016 were included.

2.2 Population, Sample size & technique and Sample selection:

The catchment area of our hospital is D.I.Khan Division, which includes D.I.Khan & Tank districts, South Waziristan Agency & Frontier Region of Darazinda. The population of the Division was estimated to be approximately 2.5 million during 2016. Assuming 47% population of adults (>19 years), it will be adult population of 1,175,000, at risk of IHD. Out of this, 6.25% were assumed to have IHD as shown by Abbas, et al.[7] i.e. 73,438 adults.

Out of this population of 73,438, a sample size of 331 was selected through an online sample size calculator Raosoft®[25], with margin of error 4.511%, 90%CL and prevalence of DM in adult IHD population as 25%. The sampling technique was consecutive non-probability.

All indoor adult (>19 years) patients of ACS were eligible. Those with other cardio-respiratory symptoms, mimicking ACS were excluded.

2.3 Data Collection Plan: Sex (men & women), age groups (up to 60 years and > 60 years), and residence (urban and rural) were demographic while presence of DM (yes and no) was a research variable (attributes). The data type for all these variables was nominal. Presence of DM was a dependent variable, while sex, age groups and residence each was an independent variable for tests of association.

2.4 Data Analysis Plan:

2.4.1 Descriptive Statistics & Estimation of Parameters: All the four variables will be described by count and percentage for the sample. The estimated parameters for population will be given as confidence interval (CI) for proportion at 95% confidence level (CL) using the normal distribution approximation for binomial distribution using an online statistical calculator.[26]

2.4.2 Hypotheses Testing: The observed and expected frequency and observed and expected distribution of DM by sex, age groups and residence respectively in adult ACS population will be substantiated by using chi-square goodness of fit test.[27,28] The association of the presence of DM to sex, age groups and residence will be substantiated respectively by chi-square test of association.[27,28] Observed

counts, expected counts, their difference, square of their difference, chi-square value, degree of freedom and significance (p-value) will be given for each test separately using an online statistical calculator.[29] All these tests will be performed at alpha .05.

A research document should be presented in a way that all its contents are not only valid and reliable, but also verifiable, replicable and repeatable. More often the global literature doesn't apply appropriate tests of significance. In case chi-square test is applied, its type (goodness-of-fit, association, McNemar, Mantel-Haesznel etc), and its steps (observed counts, expected counts, their difference, square of their difference, chi-square value, degree of freedom etc) except p-value are not given. That's why we are placing the theoretical background of the tests which we will use.

2.4.3 Chi-square goodness of fit test[27,28]: It is a univariate (single variable) test for nominal/ ordinal data, used for a 'single' group and analogous to one-sample t test for interval/ ratio (numeric) data. It is used to testify the hypothesis to see the significance of 'difference' between the observed and expected counts/ proportions (never percentages) for frequency or distribution of a disease. The observed counts/ proportions/ data are from his sample and the expected are from his population, from which he has drawn this sample. If the expected counts (parameter for proportion) for his population are unknown, he can bring these from some similar population or these may be even hypothetical for his population (from background knowledge regarding the event). The author has to tell the source of this data with reference as different expected counts will give different results.

We haven't come across a research paper in medical sciences using this proper test for comparison of frequency (observed versus expected) or distribution (observed versus expected) of a disease. This would be an innovated addition to global literature on our part.

2.4.4 Chi-square test of association (independence)[27,28]: It is used to testify the hypothesis to see the significance of 'association' between the 'two' nominal/ ordinal variables of the 'same' group. It is analogous to correlation test for interval/ ratio (numeric data). Both show the effect of one variable on another of the 'same' group, giving cause and effect relationship (determinants of disease) in a cross-sectional enquiry.

It is never a test to see the significance of difference for proportion between the 'two' groups as more often wrongly used in global literature. In fact no chi-square or any other test is there to see the significance of difference between the two or more independent (unpaired) or paired (dependent) groups for nominal/ ordinal data. With some restrictions, McNemar chi-square test is used for two (not more) independent groups with strictly equal sample sizes and strictly binary nominal data, used mostly in experimental designs.[22,30]

What is practiced more often in global literature is that they apply chi-square test of association for comparison (to see the significance of difference) of the two groups on nominal/ ordinal data. In such cases, any interpretations, discussion, comparisons, conclusions, recommendations, decisions, policies, programs and other such actions based on these results will not be valid and reliable and need to be re-visited by the concerned stakeholders.

Then what to use for comparison of frequency and distribution (by person, place and time) of a disease or a health related event? It is the chi-square goodness-of-fit test as described and used in this manuscript.

3. RESULTS

3.1 Descriptive Statistics & Estimation of Parameters:

3.1.1 Sample description & Frequency of DM in adult ACS population: Out of 331 patients with ACS, 225 (68.0%) were men and 106 (32.0%) women, 221 (66.8%) were ≤60 years and 110 (33.2%) >60 years, and 210 (63.4%) were urban and 121 (35.6%) rural.

The frequency (%) of DM in the sample was 79/331 (23.87%). The estimated prevalence of DM in adult ACS population of D.I.Khan Division lies between 19.27% and 28.45% at 95%CL. (Table 3.1.1)

3.1.2 Distribution of positive cases of DM in adult ACS population by sex, age groups & residence:

Research is an activity to solve a problem for a

Table 3.1.1: Frequency of DM in sample and prevalence in adult ACS population of D.I.Khan Division, Pakistan (n=331)

Presence of DM	Sample Statistics		95% CI for Proportion	
	Count	Percentage	Lower	Upper
Yes	79	23.87	19.27	28.45
No	252	76.13	71.54	80.72
Total	331	100.00	Population Parameters	

population, never for a sample, of course through a sample. Many authors describe their sample only with no mention of their population. They don't have any specified population and they don't infer (estimation of parameter & hypothesis testing) their sample results to their population. Strictly defined, it is not altogether research.

We have defined our population, drawn a sample, observed it thought four variables, described the sample (descriptive analysis/ sample statistics), described the population by inferring sample results to population (estimation of parameter/ inferential statistics) and then compared the observed counts of our sample to the expected counts of some other populations as seven hypotheses (hypothesis testing/ inferential statistics).

The distribution of positive cases of DM by sex, age groups and residence in adult ACS population of D.I.Khan Division is shown in Table 3.1.2. Here the frequency of DM in ACS in sample (and its estimated prevalence in population) was more in men 13.29% than women 10.58%, more in age ≤60 years 17.22% than >60 years 6.65%, and more in urban 16.01% than rural population 7.86%.

As 252 (76.13%) cases have no DM, so these cases are not included in the distribution of DM by sex, age groups and residence. Only 97 (23.87%) cases having DM are distributed.

When we compare the distribution of DM by sex or any other disease by any demographic variable/ factor (person, place & time), etc. to some other studies as needed in discussion, we often see that the distribution is done as such, say in case of our study, it would be either;

DM in men= 44*100/79=55.7% and DM in women= 35*100/79=44.3%, totaling to 100%. But it is not correct as we know that only 23.87% cases have DM, not 100%.

DM in men= 44*100/225=19.55 and DM in women= 35*100/106=33.01, totaling to 52.56%. But it is also not correct as we know that only 23.87% cases have DM, not 52.56%.

The way we have distributed is shown in Table 3.1.2. This would be an innovated addition to the global literature on our part.

3.2 Hypotheses Testing:

3.2.1 Observed vs expected frequency of DM in adult ACS population ($H_0$1):

Our observed counts for the presence of DM (Yes: No) were 79:252 from a sample of 331 against expected counts of 79:171 from a sample of 250 by Ahmad, et al.[19] With different sample sizes/ denominators, comparison was not possible. Hence the expected counts and expected percentages were adjusted for a sample of 331. The expected counts of 79:171 were replaced by 105:22 and expected percentages of 31.6%:68.4% were replaced by 31.72%:68.28%. (Table 3.2.1.1)

Table 3.1.2: Distribution of positive cases of DM by sex, age group and residence in adult ACS population of D.I.Khan Division, Pakistan (n=79/331)

Variables	Attributes	Sample size	Sample Statistics		95% CI for Proportion	
			Count	Percentage	Lower	Upper
Sex	Men	225	44	44*100/331= 13.29%	09.63	16.95
	Women	106	35	35*100/331= 10.58%	07.26	13.88
Age group	≤ years	221	57	57*100/331= 17.22%	13.15	21.28
	> 60 years	110	22	22*100/331= 06.65%	03.96	09.33
Residence	Urban	210	53	53*100/331= 16.01%	12.06	19.96
	Rural	121	26	26*100/331= 07.86%	04.95	10.75
	Total	331	79	79*100/331= 23.87%	19.27	28.45

Table 3.2.1.1: Observed, expected and adjusted expected counts and percentages for frequency of DM in ACS population of D.I.Khan Division, Pakistan (n=331)

Presence of DM	Observed Counts	Observed %	Expected Counts	Expected %	Adjusted Expected Counts	Adjusted Expected %
Yes	79	23.87%	79	79*100/250=31.6%	79*331/250=105	105*100/331=31.72%
No	252	76.13%	171	171*100/250=68.4%	171*331/250=226	226*100/331=68.28%
Total (n)	331	100%	250	100%	331	100%

Table 3.2.1.2: Observed vs expected frequency of DM in adult ACS population of D.I.Khan Division, Pakistan (n=331)

Variable	Attributes	O	E	O-E	$(O-E)^2$	$(O-E)^2/E$	χ^2	d.f.	P-value
Presence of DM	Yes	79	105	-26	676	6.44	9.43	1	.00214
	No	252	226	26	676	2.99	$H_0$1 rejected at alpha .05		
	Total	331	331	00	Chi-square goodness of fit with Yates correction				

O= Observed Counts, E= Expected Counts, χ^2= Chi-square value, d.f.= Degree of freedom

Table 3.2.2.1: Observed & expected counts and observed, expected and adjusted expected percentages for distribution of positive cases of DM by sex in ACS population of D.I.Khan Division, Pakistan (n=331)

Positive cases of DM	Observed Counts	Observed %	Expected Counts	Expected %	Adjusted Expected %
Men	44	44*100/331=13.29%	41	41*100/250=16.4%	41*100/331=12.39%
Women	35	35*100/331=10.58%	38	38*100/250=15.2%	38*100/331=11.48%
Total Positive	79	79*100/331=23.87%	79	79*100/250=31.6%	79*100/331=23.87%

Table 3.2.2.2: Observed vs expected distribution of positive cases of DM by sex in adult ACS population of D.I.Khan Division, Pakistan (n=79/331)

Variable	Attributes	O	E	O-E	$(O-E)^2$	$(O-E)^2/E$	χ^2 value	d.f.	P-value
Sex	Men	44	41	3	9	.22	0.46	1	.4993
	Women	35	38	-3	9	.24	$H_0$2 accepted at alpha .05		
	Total	79	79	00	Chi-square goodness of fit test with Yates correction				

O= Observed Counts, E= Expected Counts, χ^2= Chi-square value, d.f.= Degree of freedom

Chi-square goodness-of-fit test showed p-value less than alpha. $H_0$1 was proved to be false and hence rejected, showing that there is no good fit between the expected and observed counts. In simple words, the prevalence of 23.87% (79*100/331) of DM in our population is significantly lower than what we expected from the adjusted expected count and adjusted expected percentage of 31.72% (105*100/331) from Ahmad, et al.[19] (Table 3.2.1.2)

3.2.2 Observed vs expected distribution of positive cases of DM by sex in adult ACS population ($H_0$2):

Our observed distribution for men versus women was 44:35 out of 79 DM positive cases from a sample of 331, against an expected distribution of 41:38 out of 79 DM positive cases from a sample of 250 by Ahmad, et al.[19] Having same denominator of 79 for positive cases, no adjustment for the expected counts was required.

Percentages are not required in calculation for chi-square test, so not included in any of the seven chi-square test tables. Yet, for easy interpretation, say for comparisons in discussion, percentages are required. Percentages of expected counts from a sample of 250 are adjusted for a sample of 331. The expected percentages of 16.4%:15.2% were replaced by 12.39%:11.48%. (Table 3.2.2.1)

Chi-square goodness-of-fit test showed p-value >alpha. $H_0$2 was proved to be true and hence accepted, showing that the observations fit the statistical model of the population. In simple words, our observed prevalence of DM in men 13.29% (44*100/331) was statistically similar to what we expected for men 12.39% (41*100/331) & our observed prevalence of DM in women 10.58% (35*100/331) was similar to what we expected for women 11.48% (38*100/331) from Ahmad, et al.[19] as per adjusted percentages for expected counts. (Table 3.2.2.2)

3.2.3 Observed vs expected distribution of positive cases of DM by age groups in adult ACS population ($H_0$3):

Our observed distribution for age group ≤60 years versus >60 years was 57:22 out of 79 DM positive cases from a sample of 331 against an expected distribution of 131:92 out of 223 DM positive cases from a sample of 605 adult cases of ACS by Hussain, et al.[20] from Bahawalpur, Pakistan.

With different sample sizes/ denominators, comparison was not possible. Hence the expected counts and expected percentages were adjusted for a sample of 331. The expected counts of

Table 3.2.3.1: Observed & expected counts and expected and adjusted expected percentages for distribution of positive cases of DM by sex in ACS population of D.I.Khan Division, Pakistan (n=331)

Positive cases of DM	Observed Counts	Observed %	Expected Counts	Expected %	Adjusted Expected Counts	Adjusted Expected %
Age ≤ 60 years	57	57*100/331=17.22%	131	131*100/605=21.65%	131*79/223=46	46*100/331=13.90%
Age > 60 years	22	22*100/331=06.65%	92	92*100/605=15.21%	92*79/223=33	33*100/331=09.97%
Total Positive	79	79*100/331=23.87%	223	223*100/605=36.86%	223*79/223=79	79*100/331=23.87%

Table 3.2.3.2: Observed vs expected distribution of positive cases of DM by age groups in adult ACS population of D.I.Khan Division, Pakistan (n=79/331)

Variable	Attributes	O	E	O-E	$(O-E)^2$	$(O-E)^2/E$	χ^2 value	d.f.	P-value
Age group	≤ 60 years	57	46	11	121	2.63	6.30	1	.01209
	>60 years	22	33	-11	121	3.67	$H_0$3 rejected at alpha 0.05		
	Total	79	79	00	Chi-square goodness of fit test with Yates correction				

O= Observed Counts, E= Expected Counts, χ^2= Chi-square value, d.f.= Degree of freedom

Table 3.2.4.1: Observed, expected and adjusted expected counts and their percentages for distribution of positive cases of DM by residence in ACS population of D.I.Khan Division, Pakistan (n=331)

Positive cases of DM	Observed Counts	Observed %	Expected Counts	Expected %	Adjusted Expected Counts	Adjusted Expected %
Urban	53	53*100/331=16.01%	210	210*100/5,433=3.86%	210*79/475=35	35*100/331=10.58%
Rural	26	26*100/331=07.86%	265	265*100/5,433=4.88%	265*79/475=44	44*100/331=13.29%
Total Positive	79	79*100/331=23.87%	475	475*100/5,433=8.74%	475*79/475=79	79*100/331=23.87%

131:92 were replaced by 46:33 and expected percentages of 21.65%:15.21% were replaced by 13.90%:09.97%. It is important to note that we are distributing only 79 positives (23.87%) and not the 252 (76.13%) negative cases out of 331 (100%). (Table 3.2.3.1)

Chi-square goodness-of-fit test showed p-value less than alpha. $H_0$2 was proved to be false and hence rejected, showing that the observations don't fit the statistical model of the population. In simple words, our observed prevalence of 17.22% (57*100/331) of DM in ACS was statistically significantly higher than adjusted expected prevalence of 13.90% (46*100/331) for age group ≤60 years & our observed prevalence of 6.65% (22*100/331) of DM was statistically significantly lower than adjusted expected prevalence of 9.97% (33*100/331) for age group >60 years. (Table 3.2.3.2)

3.2.4 Observed vs expected distribution of positive cases of DM by residence in adult ACS population ($H_0$4):

Our observed distribution of DM for urban versus rural was 53:26 out of 79 DM positive cases from a sample of 331 against an expected distribution of 210:265 out of 475 DM positive cases from 5,433 adult 'healthy' persons from the four provinces of Pakistan by Shera, et al.[14] from first National Diabetes Survey of Pakistan. No study was available for distribution of DM in ACS for residence (urban/rural), hence a survey for presence of DM in healthy population was selected.

With different sample sizes/ denominators, comparison was not possible. Hence the expected counts and expected percentages were adjusted for a sample of 331. The expected counts of 210:265 were replaced by 35:44 and expected percentages of 3.86%:4.88% were replaced by 10.58%:13.29%. It is important to note that we are distributing only 79 positives (23.87%) and not the 252 (76.13%) negative cases out of 331 cases. (Table 3.2.4.1)

Chi-square goodness-of-fit test showed p-value less than alpha. $H_0$2 was proved to be false and hence rejected, showing that the observations don't fit the statistical model of the population. In simple words, our observed prevalence of 16.01% (53*100/331) of DM in ACS was statistically significantly higher than adjusted expected prevalence of 10.58% (35*100/331) for urban & our observed prevalence

Table 3.2.4.2: Observed vs expected distribution of positive cases of DM by residence in adult ACS population of D.I.Khan Division, Pakistan (n=79)

Variable	Attributes	O	E	O-E	$(O-E)^2$	$(O-E)^2/E$	χ^2 value	d.f.	P-value
Residence	Urban	53	35	18	324	9.26	16.62	1	.00005
	Rural	26	44	-18	324	7.36	$H_0$4 rejected at alpha 0.05		
	Total	79	79	00	Chi-square goodness of fit test with Yates correction				

O= Observed Counts, E= Expected Counts, χ^2= Chi-square value, d.f.= Degree of freedom

Table 3.2.5: Association of presence of DM to sex in adult ACS population of D.I.Khan Division, Pakistan (n=331)

Variables	DM-Yes	DM- No	Rows Total	Chi-square value (χ^2)	d.f.	P-value
Sex	O (E) [x^2]	O (E) [x^2]				
Men	44 (53.7) [1.75]	181 (171.3) [0.55]	225	6.4659	1	.01099
Women	35 (25.3) [3.72]	71 (80.7) [1.17]	106	Chi-square test of association with Yates correction		
Columns Total	79	252	331 (Grand Total)	$H_0$5 rejected at alpha 0.05		

DM= Presence of DM, O= Observed Counts, E= Expected Counts, d.f.= Degree of freedom

Table 3.2.6: Association of presence of DM to age groups in adult ACS population of D.I.Khan Division, Pakistan (n=331)

Variables	DM-Yes	DM- No	Rows Total	Chi-square value (χ^2)	d.f.	P-value
Age groups	O (E) [x^2]	O (E) [x^2]				
≤ 60 years	57 (52.75) [0.34]	l64 (168.25) [0.11]	221	1.0559	1	0.30416
>60 years	22 (26.25) [0.69]	88 (83.75) [0.22]	110	Chi-square test of association with Yates correction		
Columns Total	79	252	331 (Grand Total)	$H_0$6 accepted at alpha 0.05		

DM= Presence of DM, O= Observed Counts, E= Expected Counts, d.f.= Degree of freedom

Table 3.2.7: Association of presence of DM to residence in adult ACS population of D.I.Khan Division, Pakistan (n=331)

Variables	DM-Yes	DM- No	Rows Total	Chi-square value (χ^2)	d.f.	P-value
Residence	O (E) [x^2]	O (E) [x^2]				
Urban	53 (50.12) [0.17]	157 (159.88) [0.05]	210	0.4058	1	0.52411
Rural	26 (28.88) [0.29]	95 (92.12) [0.09]	121	Chi-square test of association with Yates correction		
Columns Total	79	252	331 (Grand Total)	$H_0$7 accepted at alpha 0.05		

DM= Presence of DM, O= Observed Counts, E= Expected Counts, d.f.= Degree of freedom

of 7.86% (26*100/331) of DM was statistically significantly lower than adjusted expected prevalence of 13.29% (44*100/331) for rural. (Table 3.2.4.2)

3.2.5 Association of presence of DM to sex in adult ACS population ($H_0$5):

Presence of DM in ACS as a research/ dependent variable was cross-tabulated by sex as a demographic/ independent variable. With p-value less than alpha, $H_0$5 was proved to be false and hence rejected, showing that there is association between the presence of DM and sex. (Table 3.2.5)

3.2.6 Association of presence of DM to age groups in adult ACS population ($H_0$6):

Presence of DM in ACS as a research/ dependent variable was cross-tabulated by age groups as a demographic/ independent variable. With p-value more than alpha, $H_0$6 was proved to be true and hence accepted, showing that there is no association between the presence of DM and age groups. (Table 3.2.6)

3.2.7 Association of presence of DM to residence in adult ACS population ($H_0$7):

Presence of DM in ACS as a research/ dependent variable was cross-tabulated by residence as a demographic/ independent variable. With p-value more than alpha, $H_0$7 was proved to be true and hence accepted, showing that there is no association between the presence of DM and residence. (Table 3.2.7)

4. DISCUSSION

4.1 Frequency of DM in adult ACS population ($H_0$1):

The frequency of DM in ACS in our sample was 23.87% with estimated prevalence in adult ACS population of D.I.Khan Division between 19.27%-28.45% at 95% CL.

Higher prevalence of DM in ACS than our study was shown by Ahmad et al.[19] from Abbottabad, Pakistan for the period from October, 2009 to April, 2010, as 31.6% (79*100/250) in 250 patients with ACS, and by Hussain, et al.[20] from Bahawalpur, Pakistan during June 2009-December 2011, as 36.85% (223*100/605) in 605 adult cases of IHD.

Our observed prevalence of DM in ACS 23.87% from a sample of 331 was significantly lower (p=.00214) than what we expected as 31.72% from a study by Ahmad, et al.[19] from a sample of 250.

Having different sample sizes, these figures were not comparable, so these were adjusted for a sample of 331. The expected count of 79 was replaced by 105 (79*331/250=105) and expected percentage of 31.6% (79*100/250) was replaced by 31.72% (105*100/331). (Table 3.2.1.1 & Table 3.2.1.2).

No relevant studies with hypothesis testing could be retrieved from literature for comparison.

4.2 Distribution of positive cases of DM in adult ACS population by sex ($H_0$2):

The prevalence of DM in ACS was higher in men 13.29% (95%CI 9.63-16.95) than women 10.58% (95%CI 7.26-13.88) in our population.

Similar figures are reported by Ahmad et al.[19] from Abbottabad, Pakistan, showing higher frequency of DM 16.4% (41*100/250) in men than 15.2% (38*100/250) in women, out of 250 patients with ACS.

Contrary to our results are from Hussain, et al.[20] from Bahawalpur, Pakistan showing higher frequency of DM 20.16% in women than 16.69% in men in 605 adult cases of IHD.

Our observed prevalence of DM (from a sample of 331) in men 13.29% (44*100/331) was statistically similar to what we expected for men 12.39% (41*100/331) & our observed prevalence of DM in women 10.58% (35*100/331) was similar to what we expected for women 11.48% (38*100/331) from a sample of 250 (p=.4993) by Ahmad, et al.[19]

Having same count/ denominator of 79 for positive cases, no adjustment was required for expected counts. Having different sample sizes, the percentages were not comparable, so these were adjusted for 331; the expected percentage of 16.4% (41*100/250) for men was replaced by 12.39% (41*100/331) and 15.2% (38*100/250) for women was replaced by 11.48% (38*100/331) as adjusted expected percentages. (Table 3.2.2.1 & Table 3.2.2.2)

No relevant studies with hypothesis testing could be retrieved from literature for comparison.

4.3 Distribution of positive cases of DM in adult ACS population by age groups ($H_0$3):

The prevalence of DM in ACS was higher in age group ≤60 years 17.22% (95%CI 13.15-21.28) than in age group >60 years 6.65% (95%CI 3.96-9.33) in our population.

Similar to our findings are reported by Hussain, et al.[20] from Bahawalpur (n=605), Pakistan, showing higher prevalence of 21.65% in age group ≤60 years than 15.21% in age group >60 years.

Our observed prevalence of DM in ACS for age group ≤60 years 17.22% (57*100/331) was significantly higher than expected 13.90% (46*100=331) & our observed prevalence of DM for age group >60 years 6.65% (22*100/331) was significantly lower than expected 9.97% (33*100/331) from a study by Hussain, et al.[20] (p=.01209).

Having different sample sizes/ denominators, these figures were not comparable, so these were adjusted for 331. We had 79/331 (57 men & 22 women) and Hussain, et al.[20] had 223/605 (131 men & 92 women) positive cases. The expected count of 131 for men was replaced by 46 (131*79/223=46) and of 92 for women by 33 (92*79/223=33). The expected percentage of 21.65% (131*100/605=21.65) for men was replaced by 13.90% (46*100/331=13.90) and of 15.21% (92*100/605=15.21) for women by 9.97% (33*100/331=9.97). (Table 3.2.3.1 & Table 3.2.3.2)

No relevant studies with hypothesis testing could be retrieved from literature for comparison.

4.4 Distribution of positive cases of DM in adult ACS population by residence ($H_0$4):

The prevalence of DM in ACS was higher in urban 16.01% (95%CI 12.06-19.96) than rural 7.86% (95%CI 4.95-10.75) in our population.

Contrary to our results are from Shera, et al.,[14] including 5,433 healthy subjects from all over Pakistan, showing higher frequency of 4.88% (265*100/5,433) in rural than 3.86% (210*100/5,433) in urban population, totaling to 8.74% (475*100/5,433).

Our observed frequency of DM in ACS in urban was statistically significantly higher 16.01% (53*100/331) than expected 10.58% (35*100/331) and our observed prevalence of DM in rural was statistically significantly lower 7.86% (26*100/331) than expected 13.29% (44*100/331) in healthy population from a study by Shera, et al.[14] (p=.00005).

Having different sample sizes/ denominators, these figures were not comparable, so these were adjusted for 331. We had 79/331 (53 urban & 26 rural) and Shera, et al.[14] had 475/5,433 (210 urban & 265 rural) positive cases. The expected count of 210 for men was replaced by 35 (210*79/475=35) and of 265 for women by 44 (265*79/475=44). The expected percentage of 03.88% (210*100/5,433=3.88) for men

was replaced by 10.58% (35*100/331=10.58) and of 04.88% (265*100/5,433=4.88) for women by 13.29% (44*100/331=13.29). (Table 3.2.4.1 & Table 3.2.4.2)

No relevant studies with hypothesis testing could be retrieved from literature for comparison.

4.5 Association of presence of DM to sex, age groups and residence in adult ACS population ($H_0$5-$H_0$7): There was association between the presence of DM and sex ($H_0$5) (p=0.011). There was no association between the presence of DM and age groups ($H_0$6) (p=0.3041), and presence of DM and residence ($H_0$7) (p=0.5241) in adult ACS population of D.I.Khan Division.

No relevant studies could be retrieved from literature for comparison.

5. CONCLUSION

Prevalence of DM in adult ACS population of D.I.Khan Division, Pakistan was found lower than expected. The prevalence was more in men than women, more in younger age group (≤60 years) than older age group (>60 years) and more in urban than rural population. Our prevalence of DM was lower than expected, our distribution by sex was similar to expected while our distribution for age groups and residence were not similar to expected. The presence of DM was associated to sex but not to age groups and residence in adult ACS population of D.I.Khan Division, Pakistan.

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CONFLICT OF INTEREST
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AUTHORS' CONTRIBUTION

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All the authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.