Student's Journal of Health Research Africa
Vol. 4 No. 12 (2023): December 2023 Issue
https://doi.org/10.51168/sjhrafrica.v4i12.823
Original article

A PROSPECTIVE STUDY ON ANAEMIA AS A MORTALITY RISK FACTOR IN DIABETIC AND NON-DIABETIC PATIENTS FOLLOWING ACUTE MYOCARDIAL INFARCTION.

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ABSTRACT.

Introduction:
Short-term mortality is related to hyperglycemia, acute myocardial infarction (AMI), and anemia. Diabetes patients are more likely to suffer from anemia. To investigate the impact of diabetes patients also having anemia on myocardial infarction outcomes, we conducted a retrospective study.

Methodology:
From a registry that is disease-specific and population-based, information about every patient consecutively hospitalized with AMI was gathered. Diabetes and anemia were present in four groups of patients.

Results:
32.2% of Group A, 16% of Group B, 21.45% of Group C, and 6.6% of Group D experienced 30-day mortality (all $p < 0.001$). Groups A, B, C, and D had, in that order, 31 days to 36 months mortality rates of 47.6%, 20.8%, 34.3%, and 10.4% (all $p < 0.001$). At 36 months, the odds ratios for diabetes and anemia were 1.61 (1.40–1.84, $p < 0.001$) and 1.58 (1.37–1.86, $p < 0.001$), respectively, suggesting that both illnesses remained independent risk factors for death. Of the deaths that occurred between 31 days and 36 months, 43.7% in Group A were due to cardiovascular causes, 54.0% in Group B, 47.1% in Group C, and 50.9% in Group D ($p < 0.05$, A vs. B).

Conclusion:
When compared to either diabetes or anemia patients alone, patients who have diabetes and anemia both have a greater death rate. In all groups, cardiovascular death continued to be the most common death cause.

Recommendation:
According to our findings, individuals with anemia who have experienced a myocardial infarction with or without diabetes may safely have prompt primary percutaneous coronary intervention; nevertheless, they should take extra care to maintain hemoglobin levels.

Keywords: Diabetes Mellitus, Acute Myocardial Infarction, Anemia, Congestive Heart Failure
Submitted: 2023-11-13 Accepted: 2023-11-17

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INTRODUCTION.

Both diabetes mellitus (DM) and anemia are considered essential, sole risk factors for mortality after an acute myocardial infarction (AMI) and recurrent ischemia. [1-6]. When glomerular filtration rate and iron reserves are considered, anemia is 2-3 times greater in diabetics than in non-diabetics [7].

Anemia has been linked to higher short-term death risks in ischemic heart disease (IHD) individuals, according to recent research [7, 8]. On the other hand, not much data is available about the long-term prediction of anemia in ischemic heart disease (IHD) patients. After adjusting for different confounding variables, the research found no such difference in mortality long-term linked to anemia [8].

The actual death causes associated with low hemoglobin levels are undefined because anemia is frequently a sign of an underlying illness. It's possible that these people are not dying of cardiovascular disease but instead of a related illness [9, 10]. However, the outcomes of acute MI patients who also have both anemia and diabetes have not been studied.

This study aimed to investigate anemia's effect on death, short-term and long-term morbidity, and cause-specific mortality in this patient group who had an AMI and either had diabetes mellitus or not.

METHODOLOGY.

Study Design.
The rationale and techniques of the prospective study on disease management programs have been thoroughly documented in other places [9]. For this investigation, all patients had comprehensive clinical data from skilled abstractors with AMI admitted for two years at a tertiary care center.

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Variables and Data Analysis.

The three morbidity outcomes were combined into a composite form: nonfatal myocardial infarction, readmission for uncontrolled angina or ischemic heart failure, and mortality at 30 days to 36 months. Upon admission, based on whether anemia and diabetes were present or not, there were four groups of patients. The Canadian Diabetes Association's 2003 clinical practice recommendations classified diabetes as an entrance glucose greater than 200 mg/dL or a history of diabetes [10]. The World Health Organization (WHO) defines anemia as having a level of hemoglobin in males of less than 13.1 g/dL and a level in females of less than 12.1 g/dL [11].

For data analysis, clinical characteristics and patient demographics were used to extract the following information about the patients: age, body mass index (BMI), sex, blood pressure, smoking status, type of AMI, and prior history of AMI or cardiac medicines at discharge. Serum creatinine kinase, serum creatinine, hemoglobin, lipid profile, and mean glucose were among the lab findings. The Cockroft-Gault equation was utilized to compute the clearance of creatinine.

Bias.

There was a chance that bias would arise when the study first started, but we avoided it by giving all participants identical information and hiding the group allocation from the nurses who collected the data.

Statistical Analysis.

The Chi-square tests were used for categorical data to contrast the physiological and demographic characteristics of the research groups, and ANOVA was applied to continuous variables. At a significance threshold of $p < 0.05$, the data items that were shown to differ across the research groups applied to the Cox Proportional Hazards regression framework in univariate analysis. Mortality was the relevant parameter in the model.

A backward elimination strategy was used to create the most cost-effective models that showed the relationship between the prediction and the outcome variables. All feasible predictions were entered as a block during this process. Based on how each one connected to the result, they were eliminated one at a time. Patients' hemoglobin levels for each sex were plotted into quintiles for illustrative purposes, and a 36-month survival curve was produced. SPSS 10.0 was used for all analyses (Chicago, IL).

RESULTS.

150 patients hospitalized with acute MI between the ages of two and up received therapy. (0.5%) patients were not included in the subsequent analysis due to incomplete data. Of the patients observed for a maximum of 36 months after their first hospitalization, (99.5%) patients made up the research. Based on the patients' status for diabetes and anemia, four groups were created: Those with diabetes mellitus (DM) and anemia (n =14) made up group A; those without DM and anemia (n = 38); those without DM and anemia (n = 18); and those without both DM and anemia (n = 80) made up group B.

Individuals suffering from anemia were less likely to have early-onset coronary artery disease in their families (10.8%, 13.1%, and 32.2%, regarding groups A, B, C, and D respectively). When anemia, diabetes, or both were present, the incidence of prior MI was significantly higher in groups comparatively speaking, groups A (27.89%), B (12.1%), C (18.9%), and D (4.9%) were lower than A (32.1%), B (26.12%), C (27.30%), and D (17.98%). A higher percentage of diabetes patients (groups A 63.4%, B 61.5%, C 51.3%, and D 43.8%) had a history of hypertension, according to all between-group comparisons except A vs. B, where p = ns.

To take into consideration both outcomes (short and long terms), all-cause mortality was estimated separately for deaths that happened within 30 days of admission and deaths that happened between 31 days and 36 months. Groups A, B, C, and D had short-term all-cause death rates (all $p < 0.001$) of 32.3%, 16.1%, 21.5%, and 6.6%, in that order. Groups A, B, C, and D had long-term death rates of 20.8%, 34.3%, 10.4%, and 47.67%, respectively (all $p < 0.001$) (Table 1).

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Table 1: Mortality and Morbidity.

	Group A Diabetes Anemia n = 14	Group B Diabetes No Anemia n = 38	Group C No Diabetes Anemia n = 18	Group D No Diabetes No Anemia n = 80
Mortality				
≤30 days	32.4 % ^bb, cc, dd	16.12%^aa, cc, dd	21.6%^aa, bb, dd	6.7%^aa, bb, cc
31d – 36 months (% of 30d survivors)	47.67 %^bb, cc, dd	20.8%^aa, cc, dd	34.4%^aa, bb, dd	10.5%^aa, bb, cc
Morbidity 31 days – 36 months				
Reinfarction	3.40%	2.90%	2.10%	2.40%
CHF admission	12.0%^bb, c, dd	6.71%^aa, cc, dd	8.20%^a, bb, dd	2.91%^aa, bb, cc
Unstable Angina (UA)	7.78%^bb, c, dd	15.20%^aa, c, dd	10.63%^a, b, dd	16.89%^aa, bb, cc
Composite endpoint (Reinfarction, CHF, UA)	23.0%	24.8%^c,d	20.8% ^b	22.1%^b
Morbidity ≤30 days				
Reinfarction	1.0%	0.9%	1.2%	1.0%
CHF admission	3.8%^b,c, dd	2.9%^a, dd	1.7%^a	1.4%^aa, dd
Unstable Angina (UA)	2.4%^b, dd	4.3%^a, dd	3.2%^d	5.7%^aa, bb, c
Composite endpoint (Reinfarction, CHF, UA)	7.1%	8.1%	6.1%	8.1%

**a indicates a p-value of less than 0.05 between group A and this group. For both group B and the current group, b indicates p < 0.05. P < 0.05 between group C and the present group is indicated by the letter c. In the case of group D and the current group, d indicates p < 0.05. A double sign (aa, for example) indicates p < 0.001. Rounding causes percentages to only sometimes add up to the total.*

The overall goal of treatment for unstable angina, CHF, and/or non-fatal re-infarction at 30 days was the same for all groups in terms of fatality. Group B had the highest occurrences from 31 days to the end of the study (Group (B) vs. Groups (C and D), $p < 0.05$) compared to the non-diabetic categories. Examining different morbidity components, there was no significant change in the non-fatal reinfarction hospitalization rates between 31 days and 36 months.

After adjusting for the impact of the other covariates, the variables that remained in the models were only those that had a significant connection with the result. Diabetes was considered to be the sole risk factor for death (odds ratios at 30 days were 1.45 [CI = 1.20-1.76] and 1.61 [CI = 1.41-1.85], both < 0.001). Anemia did not directly affect short-term mortality when other factors were considered. However, anemia upon admission remained a significant long-term predictor of death (OR 1.59, CI = 1.38 – 1.85).

DISCUSSION.

Our findings indicate that insufficient blood is a predictor of long-term death only, despite earlier research showing that anemia is a unique signal of short-term mortality [1, 2]. The variations in the definition of anemia and the study methodology could be one reason for this discrepancy. An unadjusted mortality study conducted on senior Medicare participants, for example, discovered a negative correlation between progressively declining hematocrit levels and 30-day mortality [12].

Our knowledge of the patient's short- and long-term risk of mortality when they present with an AMI is enhanced by the current study. There were two objectives for this investigation. Initially, our goal was to evaluate how diabetes mellitus and anemia coupled affected the prognosis of patients suffering from acute myocardial infarction. Second, we looked at the cause-specific death of anemic patients. However, our results differ significantly from those of other studies. Nevertheless, they show that in the post-MI group, anemia represents a distinct risk factor for death. [1, 2, 12].

Similarly, Lipšic et al. did not account for as many possible confounders as we did. Nevertheless, researchers did find an increase in adjusted 30-day mortality when anemia was found to have a level of hemoglobin 100 g/L [2]. Moreover, a post-hoc TIMI trials analysis revealed that until levels of hemoglobin in the blood dropped below 110 g/L, Sabatine et al. found no increase in these three outcomes among NSTEMI patients: myocardial

infarction, cardiovascular death, or recurrent ischemia [1]. In our investigation, hemoglobin levels of less than 120.1 g/L for females and less than 130.1 g/L for males were deemed anemic. Whether or not a person has been diagnosed with diabetes, a person's lowest hemoglobin percentile, regardless of gender, is where anemia has the most impact on survival.
Variations in the frequencies of transfusions between the groups could also explain this discrepancy. According to a recent investigation, blood transfusion may hurt acute coronary syndrome [13]. Regarding the frequency of blood transfusions for these individuals, we needed more information.

In our study, both anemic groups had significantly higher 36-month mortality rates. Nearly 65% of patients died within 36 months when they had both anemia and diabetes, which was linked to a considerable death risk. There could be other contributing factors to the elevated long-term mortality. It has been demonstrated that anemia is well tolerated in a heart that usually functions [14]. The diminished blood's ability to carry oxygen is made up for by an increased cardiac output brought on by a faster heartbeat, a more considerable stroke volume, and a decrease in blood viscosity [15-17].
A notable strength of our research is the collection of data from a sizable, contemporary cohort of patients hospitalized one after the other throughout a whole healthcare system. Also, there was a wealth of clinical detail in the gathered data.

CONCLUSION.

In a vast sequential, unselected cohort of AMI hospitalized patients, we have shown that diabetes mellitus is a significant sole risk factor for both short-term and long-term deaths. As a dichotomous variable, anemia does not independently predict 30-day death, as demonstrated by our research. This is comparable to diabetes. Conversely, anemia has been linked to a lower chance of long-term survival; the 30-month death rate increases with the degree of anemia. This is the first study that, as far as we are aware, demonstrates that anemia of any kind negatively affects long-term mortality following myocardial infarction on its own.

Anemia and diabetes together are very harmful because, at 36 months, 65% of patients in this group had passed away. It has also been discovered that cardiovascular disease, rather than other illnesses like cancer, bleeding, or renal failure, is the leading cause of death for anemia sufferers. If treating anemia can lower the mortality rate in admitted AMI individuals, more research is required to make that determination.

LIMITATIONS.

- The limitations of this study include a small sample population who were included in this study.
- Furthermore, the lack of a comparison group also poses a limitation for this study's findings.

GENERALIZABILITY.

The findings of this study cannot be generalized for a larger sample population.

RECOMMENDATIONS.

According to our findings, individuals with anemia who have experienced a myocardial infarction with or without diabetes may safely have prompt primary percutaneous coronary intervention; nevertheless, they should take extra care to maintain hemoglobin levels.

ACKNOWLEDGMENT.

We acknowledge all the technicians and staff who collect samples to detect hemoglobin levels.

LIST OF ABBREVIATIONS.

AMI - Acute Myocardial Infarction
DM - Diabetes Mellitus
IHD - Ischemic Heart Disease
BMI - Body Mass Index
MI- Myocardial Infarction

SOURCE OF FUNDING.

The study was not funded.

CONFLICT OF INTEREST.

There is no conflict of interest.

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Publisher details.

Publishing Journal: Student's Journal of Health Research Africa.
Email: studentsjournal2020@gmail.com or admin@sjhresearchafrica.org

(ISSN: 2709-9997)

Publisher: SJC Publishers Company Limited
Category: Non-Government & Non-profit Organisation
Contact: +256775434261(WhatsApp)
Email: admin@sjpublisher.org
Website: https://sjpublisher.org
Location: Wisdom Centre Annex, P.O. BOX. 701432 Entebbe, Uganda, East Africa.