Sex differences in Anaemia and its associated factors among Diabetes Mellitus in Southern Indian States

Neha Shri[1], Saurabh Singh[2], Deepanjali Vishwakarma[3], Santosh Kumar Sharma[4]*, Gudakesh[5] and Mordhwaj Pratap Singh[6]

Abstract

Anemia, a common accompaniment to diabetes is one of the major complications among diabetic patients manifesting due to renal insufficiency. However, the mechanism involved in exacerbating the risk of anemia among diabetic population is quite unclear. Moreover, the symptoms of diabetes and anemia are overlapping making it difficult to identify the presence of the disease. This study aimed to understand the sex differences in the prevalence of anemia among diabetic individuals in Southern Indian states. The study comprised diabetic individuals aged 15-49 years from the National Family Health Survey 2019-21. Bivariate and logistic regression analysis was done to identify the prevalence and factors affecting anemia among diabetic individuals. The prevalence of anemia was substantially higher among females with diabetes (51.6%) than for males with diabetes (15%). In the unadjusted model, the relative odds ratio (ROR) showed that the risk of anaemia among females with diabetes mellitus was 1.26 times higher than among males with diabetes mellitus. Further, in the model adjusted for background characteristics and behavioral factors, the risk of having anemia was 23% higher among diabetic females in comparison to their male counterparts. The high prevalence of anemia among diabetic population especially among women poses a serious public health burden. Proper identification of anemic individuals and screening them for diabetes at an early stage can help reduce the severity of complication. Maintaining glucose levels among diabetic population and improving awareness about potential risk of anemia and other complications will help reduce the burden.

Key words: Anaemia; Diabetes; Sex differential; South India.

Introduction

Diabetes Mellitus is a condition where insufficient production of the insulin hormone causes a raised level of glucose level in the blood (Roglic G., 2016). Although considered the disease of predominantly rich nations, it has now stretched its grip to a majority of middle-income countries with one-tenth of every individual suffering from the disease worldwide (WHO, 2016). More importantly, 81 percent of individuals with diabetes live in low and middle-income countries (Flood et al., 2021). The World Health Organization reported that the global prevalence of diabetes quadrupled in the period 1980-2014 (WHO, 2016) and its prevalence is predicted to rise to 643 million by 2045 (IDF). With about 6.7 million deaths by diabetes in the year 2021 (IDF, 2021),

* *Corresponding Author*
[1] *Research Scholar, International Institute for Population Sciences, Mumbai, India, Email Id: nshri793@gmail.com*
[2] *Research Scholar, International Institute for Population Sciences, Mumbai, India, Email Id: sorophd@gmail.com*
[3] *Research Scholar, International Institute for Population Sciences, Mumbai, India, Email Id: deepanjali.vishwakarma7@gmail.com*
[4] *Research Fellow, The George Institute for Global Health, New Delhi, India, Email Id: santoshiips88@gmail.com*
[5] *Assistant Professor, Population Research Centre, Institute of Economic Growth, Delhi, India Email Id: gudakesh@iegindia.org*
[6] *Assistant Professor, Department of Yogic Sciences, Lakshmibai National Institute of Physical Education Gwalior, Email Id: msingh@lnipe.edu.in*

diabetes is identified as the leading cause of mortality and reduced life expectancy. Type 2 diabetes is a multifactorial etiology including genetic and lifestyle factors (Radha & Mohan., 2007), and is still a major contributor to the occurrence of atherosclerosis (Van Dieren et al., 2010), cardiovascular disease (CVD), micro and macrovascular consequences, and kidney failure (Dev & Babitt., 2017). Although it is widely recognized that the incidence and impacts of diabetes can be prevented or reduced, around 44 percent of adult diabetes cases are undiagnosed (PAHO 2013).

Anemia is a condition where the number of red blood cells is inadequate to meet the physiological needs of the human body (WHO, 2011) is a serious public health problem affecting over 1-2 billion individuals globally in 2016 (Vos et al., 2017). With the wide recognizance that iron deficiency anaemia and type 2 diabetes mellitus (T2DM) are global health issues [Van Dieren et al., 2010], a number of studies examining the relationship between anemia and diabetes (Wright et al., 2014; Atlaw & Tariku., 2021; Mokgalaboni & Phoswa., 2022) have been conducted. Moreover, it is well established that anemia is highly prevalent in patients with diabetes and chronic kidney failures. Anemia is one of the complications among diabetic patients (Rani et al., 2010) and diabetes is one of the common causes of anemia (Al-Khoury et al., 2006) has been widely recognized however, the mechanism is unclear.

One of the most acceptable causes of anemia among diabetic individuals is "end-stage renal disease" which has been termed a "medical catastrophe" of worldwide dimension (Zhang et al., 2020; Donate-Correa et al., 2020). Diabetes is the most frequent cause of end-stage renal disease (Collins et., 2012, 2002) and causes renal anemia. Additionally, anemia, a common accompaniment to diabetes (Hizomi et al., 2023; Das and Kumar, 2022), appears earlier among diabetic patients than in those with renal impairment due to other conditions (Marathias et al., 2020). According to research, diabetic patients with renal insufficiency have a higher chance of getting anemia than diabetics with adequate kidney function because their kidneys' capacity to manufacture erythropoietin decreases. Additionally, diabetic neuropathy alters the hormone necessary for RBC synthesis, causing anaemia. In addition to renal failure, the multifactorial aetiology of anaemia in diabetes also includes autoimmune illnesses, medications, hormonal abnormalities, and nutritional deficits (Abatel et al., 2013). The mechanism through which diabetes can exacerbate anemia is through decreased iron absorption, gastrointestinal bleeding, and diabetic complications (Christy et al., 2014); systematic inflammation, damage to the renal interstitium, denervation of the kidney, drugs, altered iron metabolism and hyperglycemia (Craig et al., 2005). Additionally, studies have also reported reduced levels of serum erythropoietin, low testosterone levels, bone marrow suppression (Bhatia et al., 2006); higher serum urea and creatinine levels, lower estimated glomerular filtration rates (Goldhaber et al., 2009); and nutritional deficiencies (Bolen et al., 2011) resulting in the high prevalence of anemia among diabetic populations. The other physiological factors identified by researchers across the world are older age (Goldhaber et al., 2009).

With 67.8 million diabetic individuals, India is home to one in seven of all adults living

with diabetes in the world and more than half of the diabetes cases are undiagnosed in the country. Moreover, India ranks first in the list of the top five countries with deaths due to diabetes (Lin et al., 2020). Additionally, in the period 1990-2016, diabetes had the largest age-standardized rise in DALYs among the NCDs in India, at 39.6% (Tandon et al.,2018). Additionally, around one in every five men and 54 percent of women of reproductive ages were anemic in the country (IIPS &ICF, 2019-21). Anemia in India has a complex and population-specific etiology. Anemia in India is mainly driven by poor access to nutrition (Anand et al., 2014), and parasitic infections which lower gastric acidity relative to populations of European descent (Madhavan & Vasuprada., 2009). Additionally, Southern Indian states have the highest prevalence of diabetes in the nation despite having one of the longest-running and most effective social protection regimes in the nation, particularly concerning food and nutrition programmes (Ramamoorthy et al., 2022).

According to the NFHS-5 (2019-21) report, anemia prevalence is lower in the south region than in the other regions of India, yet around half of individuals have anemia (IIPS and ICF macro, 2021). Most type 2 diabetes patients do not know they have anaemia since the two conditions overlap symptoms like pale skin, chest pain, numbness or coldness in the extremities, shortness of breath, and headache (Alsayegh et al., 2017). Since anaemia can affect people of all ages and genders, it is necessary to conduct regional and context-specific studies to better understand the prevalence trends and risk factors among general populations in southern India. Against this backdrop, two research questions emerged, (1) what is the prevalence of anaemia among males and females and, (2) what are the factors for sex differentials in the prevalence of anemia among the diabetic population? The specific objective of the study is to understand the prevalence and predictors of anaemia in individuals with diabetes. The study hypothesizes that there is no significant difference in the prevalence of anaemia among males and females with diabetes.

Methods

Study sample

The present study utilizes data from the fifth wave of the Indian Demographic Health Survey, commonly known as the National Family Health Survey (NFHS-5), which is cross-sectional in nature and conducted in 2019-21 under the stewardship of the Ministry of Health and Family Welfare (MoHFW), Government of India and International Institute for Population Sciences (IIPS) act as a nodal agency. It is a nationally representative survey that comes up with details on fertility, infant and child mortality, maternal and child health, family planning, and various health and nutrition for each state and union territory of India. The clinical, anthropometric, and biochemical (CAB) components provide vital information on malnutrition, anaemia, high blood glucose level, and various other components via biomarker assessments.

The samples of NFHS-5 were selected using a stratified two-stage sample using the latest census (Census 2011) as a sampling frame for the selection of Primary sampling units (PSUs). Villages and Census Enumeration Blocks (CEBs) are PSUs in rural and urban areas, respectively, and were selected using probability proportional to size within each stratum. Detailed information on the sampling design of the NFHS-4 and NFHS-5 is available elsewhere (IIPS and ICF macro, 2021). This survey represents a sample of

724,115 eligible women aged 15 to 49 years from 28 states and eight union territories with a response rate of 97 percent. The current study used an individual file and a biomarker file. Since this study is focused on only southern states of India, a total of 1,20,233 samples (13,444 men aged 15-49 and 1,06,789 non-pregnant women aged 15-49) were included in the analysis for the present study.

Variables

Outcome variable

The outcome variable for this study is anaemia among the diabetes mellitus population in southern states of India. Anaemia was tested using a battery-operated portable HemoCue Hb 201+ analyser while an Accu-Chek Performa glucometer with glucose test strips was used for blood glucose. According to World Health Organization criteria, if the hemoglobin level in men and women were less than 13 g/dL and 12 g/dL respectively, then it was recorded as anaemia otherwise not. Similarly, if the individual had a blood glucose level higher than 140mg/dL or they responded as having been diagnosed with diabetes or were consuming medication for lowering blood glucose were considered diabetic otherwise not. The prevalence of anemia and diabetes by States/UTs of India according to sex is presented in Table 1.

Covariates

The study assessed various socio-economic and demographic covariates based on the previous study. The respondents' ages were categorized into 15-24 years, 25-34 years and 35-49 years. Other predictor variables included education (no education, primary, secondary and higher), marital status (never married, married and others), religion (Hindu, Muslim and others), Caste (Scheduled Castes / Scheduled Tribes, Other Backward Castes and others). Behavioral factors like alcohol consumption and tobacco smoking were dichotomized into yes and no. Body mass index was calculated as weight in kg divided by the square of height in meters and classified as per WHO guidelines as thin if BMI <18.5kg/ m2, normal if BMI ranges from 18.5 to 24.9 kg/m2 and overweight or obese if BMI >25 kg/m2. NFHS included a 'wealth score' based on the standard household assets and housing quality indicators which was derived into 5 categories: poorest, poorer, middle, richer and richest using principal component analysis. Place of residence was dichotomized into rural and urban areas.

Statistical Analysis

A descriptive analysis was used to describe the distribution of the study population stratified by sex. Bivariate analysis was performed to show the prevalence of anaemia among respondents with diabetes mellitus separately for each sex. The relationship between the dependent and independent variables was checked by using Pearson's chi^2 test. Logistic regression was performed to derive the adjusted and unadjusted odds ratios (OR) and 95 percent confidence interval. Additionally, subgroup analyses were performed to identify the factors affecting anaemia among individuals with diabetes mellitus. Further, the female-to-male ratio of odds ratios was calculated.

An interaction term was added to the logistic regression model to obtain the female-to-male ratio of odds ratio estimate (RORs) and its 95 percent Confidence Intervals (CIs). This interaction model included all main effects and their interaction with sex, otherwise, the adjustments made in the interaction model will not vary by sex, as they do in the sex-specific models. The odds

ratio (OR) for whatever sex is chosen as the reference group will be immediately generated by the interaction model, together with the ratio of odds ratios (RORs) contrasting the other sex with the reference sex. For example, if men are used as the reference group, we will get the male OR and the female-to-male RORs (together with their 95% CIs) (Woodward, 2019). Men are used as the reference group in this study. A Variance Inflation Factor (VIF) was used to assess multicollinearity between the selected predictors before executing the final model and the value of VIF is 2.2 in both the surveys, which is less than 10. All the statistical analyses were conducted by Stata®17 MP version (StataCorp LLC, Lakeway Drive College Station, Texas, USA), using the individual sampling weight variables in the dataset.

Table 1 Prevalence of Anaemia and diabetes by States/UTs of India by sex, NFHS-5 (2019-21)

	Anaemia		Diabetes (%)	
States/UTs	Male (%)	Female (%)	Male (%)	Female (%)
Jammu & Kashmir	26.9	55.9	4.6	5.6
Himachal Pradesh	14.3	45.9	8.0	8.2
Punjab	22.0	59.0	9.1	8.0
Chandigarh	7.3	59.7	11.5	11.9
Uttarakhand	13.1	38.6	11.8	7.1
Haryana	18.4	60.9	9.2	8.0
NCT of Delhi	12.9	50.9	9.1	7.0
Rajasthan	23.1	54.8	5.5	4.3
Uttar Pradesh	21.5	51.0	8.8	7.2
Bihar	29.2	63.8	10.8	9.0
Sikkim	16.3	34.7	12.0	8.4
Arunachal Pradesh	17.9	35.9	9.7	7.4
Nagaland	8.2	24.0	8.1	6.0
Manipur	5.7	29.0	10.7	8.2
Mizoram	11.4	33.6	11.8	9.1
Tripura	36.8	67.2	18.4	13.4
Meghalaya	22.2	50.7	13.1	7.7
Assam	35.8	66.2	13.2	9.5
West Bengal	38.4	71.4	16.7	12.7
Jharkhand	29.4	65.7	11.7	7.3
Odisha	28.9	64.5	12.3	9.8
Chhattisgarh	27.3	61.1	8.2	6.2
Madhya Pradesh	22.2	54.7	9.2	6.1
Gujarat	26.7	65.3	10.3	10.0
Dadra & Nagar haveli	24.4	63.4	21.1	9.3
Maharashtra	22.5	54.6	9.3	6.7
Andhra Pradesh	16.4	58.9	14.4	11.3
Karnataka	20.1	48.8	9.6	7.8
Goa	11.9	39.3	17.2	10.6
Lakshadweep	5.9	26.1	14.2	8.7
Kerala	17.2	36.5	13.2	12.1
Tamilnadu	14.9	53.1	15.4	14.6
Puducherry	19.1	56.1	13.7	12.7
Andaman & Nicobar Island	17.7	57.3	15.3	11.0
Telangana	15.3	57.7	13.5	8.9
Ladakh	28.0	42.4	12.4	7.7

Source: NFHS-5

Results

Table 2 shows the sex-wise distribution of the study population. The sample comprised 13,444 males and 1,06,789 females of which 1,761 males and 11,601 females were diabetic. Around two-fifths of the sample were aged 35-49 years. The majority of the individuals had a secondary level of education i.e., 59 percent and 54percent among males and females respectively. The proportion of married individuals, not alcoholics and non-smokers were high across both sexes.

Table 2 Socio-demographic profile of the respondents in the Southern States of India, 2019-21

Background Characteristics	Male		Female		Total	
	N	%	N	%	N	%
Age						
15-24	3,912	28.2	28,658	28.1	32,570	28.1
25-34	3,964	30.6	31,646	32.3	35,610	32.1
35-49	5,568	41.3	46,485	39.5	52,053	39.7
Education						
No education	1215	8.9	20,545	16.1	21760	15.3
Primary	1175	9.5	10,831	10.2	12006	10.1
Secondary	7944	59.3	55,476	53.8	63,420	54.5
Higher	3110	22.3	19,937	19.9	23,047	20.1
Marital Status						
Never married	5236	36.5	22,620	20.6	27,856	22.4
Married	8057	62.5	77,263	74.4	85,320	73.0
Widowed/divorced/separated/deserted	151	1.0	6,906	5.1	7057	4.6
Religion						
Hindu	10,981	82.5	86,497	81.8	97,478	81.9
Muslim	1,494	11.4	12,604	11.6	14,098	11.5
Others	969	6.2	7,688	6.6	8,657	6.6
Caste						
Scheduled caste/Scheduled tribe	4,042	28.2	32,250	28.9	36,292	28.9
OBC	7,584	59.1	59,265	57.1	66,849	57.3
Others	1,818	12.7	15,274	14.0	17,092	13.8
Place of residence						
Urban	4,598	37.8	36,987	39.6	41,585	39.4
Rural	8,846	62.2	69,802	60.4	78,648	60.6
Wealth quintile						
Poorest	659	4.0	5,514	4.1	6,173	4.1
Poorer	2,208	14.1	18,282	15.1	20,490	15.0
Middle	4,038	29.1	30,981	27.6	35,019	27.8
Richer	4,044	32.0	31,365	31.1	35,409	31.2
Richest	2,495	20.8	20,647	22.1	23,142	21.9
Consume Alcohol						
No	9,976	78.3	1,04,960	99.2	1,14,936	96.9
Yes	3,468	21.7	1,829	0.8	5,297	3.1
Consume Smoke/Tobacco						
No	10,780	82.5	1,02,748	97.6	1,13,528	95.9
Yes	2,664	17.5	4,041	2.4	6,705	4.1
Body mass index (BMI)						
Thin	1,884	13.9	16,583	15.6	18,467	15.4
normal	7,257	52.9	55,452	50.4	62,709	50.7
Overweight/obese	4,303	33.2	34,754	34.1	39,057	34.0
Anaemia*						
No	11,188	82.9	52,090	48.7	63,278	52.5
Yes	2,256	17.1	54,699	51.3	56,955	47.5
Diabetes**						
No	11,683	87.0	95,188	89.0	1,06,871	88.8
Yes	1,761	13.0	11,601	11.0	13,362	11.2
Total	13,444	100.0	1,06,789	100.0	1,20,233	100.0

*Anaemia was defined as Hb levels of < 13 g/dL in men and < 12 g/dL in women; **An individual was ascertained as having diabetes if they had high blood glucose (above 140 mg/dL) or if they were diagnosed with diabetes or if they consumed medication for lowering blood glucose.

Around 60 percent of the respondents resided in rural areas and the majority of the study participants followed Hinduism and belonged to Other Backward Castes for both sexes. Half of the respondents either male or female had normal BMI. Around one-fifth of the male (17%) and half of the females (51%) were anaemic. Further, 13 percent of males and 11 percent of females were diabetic respectively.

Table 3 shows the prevalence of anaemia among males and females with diabetes by socio-demographic characteristics. The prevalence of anaemia was highest among men aged 15-24 years while it did not vary much across ages among females. The prevalence of anaemia was higher among females without education (54.1%) while among men the prevalence was highest among men with a secondary level of education.

Table 3 Prevalence of anaemia among participants with diabetes mellitus according to sex in the Southern States of India, 2019-22

Background Characteristics	Male (N=1761)				Female (N=11601)			
	Not anaemic (%)	Anaemic (%)	n	p-value	Not anaemic (%)	Anaemic (%)	n	p-value
Age								
15-24	77.8	22.2	175		47.9	52.1	1,175	
25-34	87.3	12.7	411	0.011	47.2	52.8	2,860	0.199
35-49	85.3	14.7	1175		49.0	51.0	7,566	
Education								
No education	84.7	15.3	182		45.9	54.1	2,107	
Primary	86.0	14.0	208	0.863	48.3	51.7	1,621	0.063
Secondary	84.4	15.6	1052		48.2	51.8	6,104	
Higher	86.7	13.3	320		52.1	47.9	1,769	
Marital Status								
Never married	79.6	20.4	286	0.072	48.6	51.4	909	0.669
Married	86.0	14.0	1460		48.4	51.6	9,774	
Widowed/divorced/ separated/deserted	97.1	2.9	16		48.4	51.6	918	
Religion								
Hindu	85.5	14.5	1478	0.530	47.2	52.8	9,230	0.000
Muslim	80.9	19.1	166		56.5	43.5	1,410	
Others	84.6	15.4	117		48.5	51.5	961	
Caste								
Scheduled caste/ Scheduled tribe	85.0	15.0	483		46.3	53.7	3,148	
OBC	84.5	15.5	1057	0.874	48.5	51.5	6,731	0.016
Others	87.6	12.4	221		52.0	48.0	1,722	
Place of residence								
Urban	86.1	13.9	728	0.091	49.5	50.5	5,174	0.043
Rural	84.3	15.7	1033		47.6	52.4	6,427	
Wealth quintile								
Poorest	78.6	21.4	56		42.0	58.0	323	
Poorer	80.5	19.5	229	0.005	42.9	57.1	1,333	0.000
Middle	86.4	13.6	444		45.0	55.0	2,920	
Richer	85.3	14.7	619		49.9	50.1	3,887	
Richest	86.6	13.4	412		52.7	47.3	3,139	
Consume Alcohol								
No	84.2	15.8	1267	0.610	48.4	51.6	11,509	0.878
Yes	87.2	12.8	494		51.3	48.7	92	
Consume Smoke/Tobacco								
No	85.2	14.8	1383	0.737	48.4	51.6	11,305	0.236
Yes	84.4	15.6	378		48.6	51.4	296	
Body mass index (BMI)								
Thin	77.5	22.5	104		37.2	62.8	702	
normal	83.7	16.3	790	0.000	46.9	53.1	4,474	0.000
Overweight/obese	87.2	12.8	867		50.7	49.3	6,425	
Total	85.0	15.0	1761		48.4	51.6	11,601	

Among men, the prevalence of anemia was highest among those who never married (20.4%), Muslim religion (19.1%), OBC (15.5%), rural residents (15.7%) and those from the poorest wealth quintile (21.4%). Similarly, females from the Hindu religion (52.8%), SC/ST caste (53.7%), rural area (52.4%), and poorest wealth quintile (58%) had the highest prevalence of anemia than their respective counterparts. Further, anemia prevalence was higher among men and women who did not consume alcohol or had a thin body mass index.

The prevalence of anemia was substantially higher among females (51.6%) than for males (15%) (Fig. 1).

Figure 2 shows adjusted and unadjusted female to male ratio of odds ratios (RORs) for anaemia associated with diabetes mellitus. In the unadjusted model, ROR = 1.26 (1.08-1.46) shows that the risk of anaemia among females with diabetes mellitus was 26 percent higher than among males with diabetes mellitus.

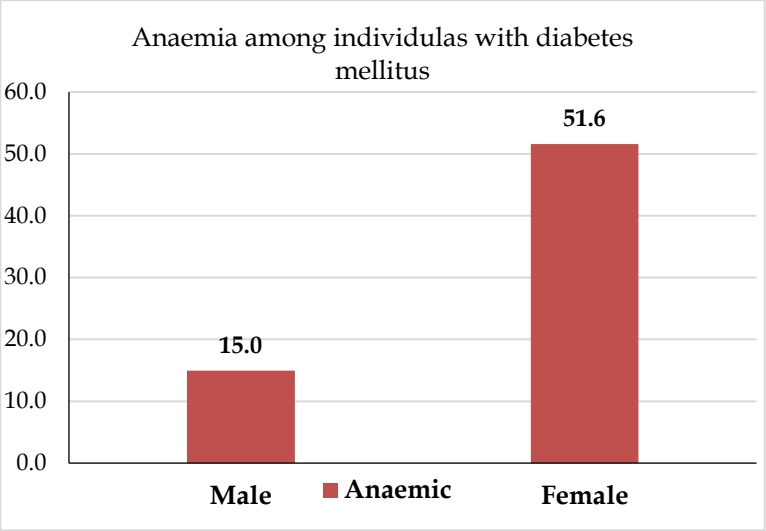


Figure 1 Prevalence of anaemia among diabetes mellitus participants by sex in Southern states of India, 2019-21

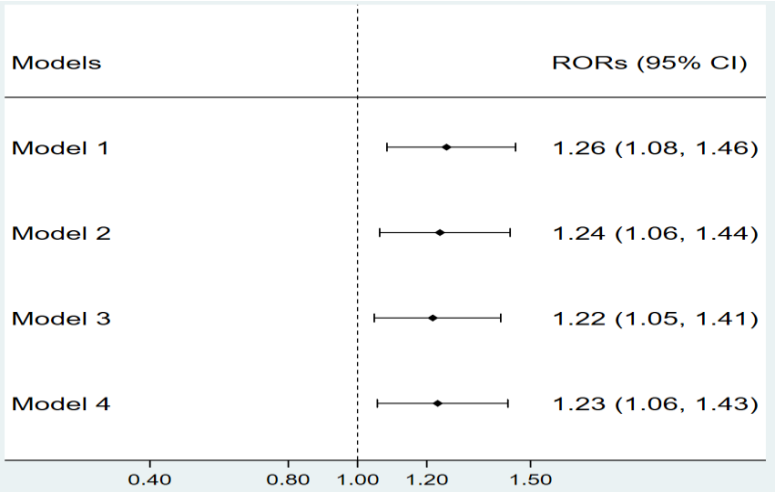


Figure 2 Female-to- male ratio of odds ratios (RORs) for Anaemia associated with diabetes mellitus among adults aged 15-49 in Southern states of India, 2019-21

Model 1: unadjusted; **Model 2**: adjusted for age, education, marital status, religion, caste, place of residence, wealth quintile; **Model 3:** consumed alcohol, smoked tobacco, body mass index; **Model 4**: adjusted for age, education, marital status, religion, caste, place of residence, wealth quintile, consumed alcohol, smoke tobacco, body mass index; **RORs (95% CI):** ratio of odd ratios in female with diabetes and odds ratios in male with diabetes with 95% confidence interval

After adjusting various background characteristics (model 2), and behavioral factors (model 3) and adjusting both background and behavioural factors (model 4) (Figure S1), risk of having anaemia associated among females was 24 percent, 22 percent, and 23 percent higher than the male with diabetes mellitus respectively. The significant risk factors for sex differentials in prevalence of anemia among the diabetic population were married, Muslims, who consume alcohol, and belonging to poorer to richest wealth quintiles of population (Figure S1).

Discussion

In this study, we found the prevalence of anemia to be 15 percent among males and 51.6 percent for females with diabetes mellitus. Studies have reported the association between DM and anemia and anemia prevalence to be higher among people with DM than in the non-DM group (Kim et al., 2021). Physical inactivity, diabetic nephropathy, poor glycemic control, recent blood loss history, and diabetes duration have been established as risk factors for anaemia in T2DM patients (Bekele et al, 2019). The prevalence of anemia among sampled diabetic individuals differed substantially from reported in other studies (Solomon et al., 2022). For instance, Aldallal & Jena (2018) reported the anemia prevalence as 22 percent and 39 percent among diabetic males and females respectively. Similarly, Alsayegh et al (2017) reported the prevalence of anemia as 36 percent and 21 percent in diabetic females and diabetic males respectively. The difference in the prevalence of anemia among the diabetic population can be attributed to lifestyle differences, variations in tools used to measure hemoglobin, poverty, nutrition, lack of awareness and illiteracy. Additionally, usage of metamorfin among diabetic individuals interferes with cyanocobalamin absorption resulting in a metformin-induced vitamin B12 deficiency and thus increases the odds of being anemic (Katroth et al., 2018). Our finding that the prevalence of anemia was substantially higher among diabetic females than diabetic males was in line with previous studies (Aldallal & Jena., 2018; Alsayegh et al., 2017; Solomon et al., 2022). Females may have a higher prevalence of anaemia due to poor nutrition and a lack of empowerment, as well as a lack of priority placed on their health. This can be enhanced through educational interventions such as rural health awareness initiatives, the provision of iron-rich foods, the prescription of vitamin and iron supplements, and awareness of diabetic consequences (Rizvi & Nishtar., 2008). Additionally, these male-female differences can also be caused by blood loss in the form of menstruation among females.

The study also found that the prevalence of anaemia was higher among young men aged 15-24 years, never married and Muslim religion. To address the higher prevalence of anemia among men aged 15-24 years in South India or any other region, would require a multi-faceted approach. This could include improving nutrition and dietary diversity, enhancing healthcare access, promoting awareness about anemia and its prevention, and addressing specific factors like hookworm infections if they are contributing to the problem. Additionally, conducting local surveys and studies to understand the specific factors contributing to the higher prevalence would be essential for designing targeted interventions (Khatri, 2017). Limited awareness about anemia and its prevention, as well as limited access to healthcare, can lead to higher prevalence

rates. Young men might not seek medical attention for symptoms of anemia, and healthcare services in some regions might not prioritize anemia prevention and treatment in this age group.

According to recent research, the presence of renal insufficiency is the most common cause of anaemia in diabetic individuals. As a result, diabetic patients have more anaemia for their level of renal impairment than non-diabetic individuals with other types of renal failure (Hizomi et al, 2023; Marathias et al., 2020). Systemic inflammation, renal interstitium damage, severe symptomatic autonomic neuropathy causing efferent sympathetic denervation of the kidney and loss of appropriate erythropoietin, drugs, altered iron metabolism, and hyperglycemia have all been proposed as reasons for the earlier onset of anaemia in diabetic patients (Craig et al., 2005). Likely, people with a longer duration of diabetes and being treated with insulin and diabetes-related complications increase their anemia levels (Goldhaber et al., 2009). However, evidence is suggestive of the fact that type 2 diabetes mellitus patients have an increased risk of developing anemia (Mokgalaboni & Phoswa., 2022).

Further, it was found that when confounded by other background and behavioral factors, the risk of having anemia decreased marginally among diabetic individuals with the relative odds ratio being higher for females. Previous studies have reported an increase in anemia prevalence with increasing age causes a subsequent deficiency of vitamins and an increasing number of comorbidities. Moreover, in line with our findings, Kim and colleagues noted a significant association in the interaction between sex and DM on the development of anemia (Kim et al., 2021). While it is unknown whether treating anaemia is beneficial for diabetic patients, DM is known to cause a variety of complications, including diabetic nephropathy and cardiovascular disease, as well as an increase in hospitalization and mortality rates. As a result, ongoing care and treatment of diabetes is critical.

Limitations and strength

Our study has a few limitations. The time between diabetes diagnosis and the start of anaemia was not known due to the cross-sectional nature of the data. As a result, the optimal time for anaemia screening remains unclear or ambiguous. Further, we have not included information regarding any diseases or drug histories that could alter the anemia and diabetes. Additionally, the causal relationship between DM and anemia must be interpreted with caution. Moreover, anemia onset involves diverse and complex mechanisms, however, the NFHS survey measures anemia based on Hb level thus making it difficult to identify other risk factors such as B12 level. Despite the limitations, the present study provides substantial evidence of the anemia prevalence among diabetic individuals within the Indian territory. Further, the use of a nationally representative dataset in this study is a major strength. This study was not limited to individuals on diabetes medication and included all individuals with diabetes. Further, we adjusted for various confounding factors such as alcohol usage, BMI, age, education, residence, and wealth.

Conclusions and recommendations

Our study reported a high prevalence of anemia among the diabetic population with more than half of the anemic women being

diabetic. Married, Muslim religion, consuming alcohol, and wealth quintiles are the major risk factors for the sex differentials in the prevalence of anemia among diabetics. Thus, proper identification of anemic individuals and screening them for diabetes especially females at an early stage can help reduce the severity of the complications. Since anemia can be easily prevented by vitamins and iron supplements improving and investing in various programs and policies aimed at reducing the undernutrition burden in the country will be crucial. Further, maintaining glucose levels among the diabetic population and improving awareness about the potential risk of anemia and other complications will help reduce the burden.

Acknowledgments

The Authors are thankful to all the coordinators of the National Family Health Survey (NFHS-5), 2019–21 for their relentless support in providing community-based estimates at National and Sub-national levels.

Data Availability

NFHS-5 (2019-21) data associated with this study is available in the public domain at the URL:
https://www.dhsprogram.com/Data/

Conflict of Interest

The authors of this paper declare that they have no conflict of interest.

Funding

This research received no specific grant from any funding agency, commercial entity, or not-for-profit organization.

References

AlDallal, S. M., & Jena, N. (2018). Prevalence of anemia in type 2 diabetic patients. Journal of hematology, 7(2), 57.

Al-Khoury, S., Afzali, B., Shah, N., Covic, A., Thomas, S., & Goldsmith, D. J. (2006). Anaemia in diabetic patients with chronic kidney disease—prevalence and predictors. Diabetologia, 49, 1183-1189.

Alsayegh, F., Waheedi, M., Bayoud, T., Al Hubail, A., Al-Refaei, F., & Sharma, P. (2017). Anemia in diabetes: experience of a single treatment center in Kuwait. Primary care diabetes, 11(4), 383-388. doi:10.1016/j.pcd.2017.04.002

Anand, T., Rahi, M., Sharma, P., & Ingle, G. K. (2014). Issues in prevention of iron deficiency anemia in India. Nutrition, 30(7-8), 764-770. doi: 10.1016/j.nut.2013.11.022.

Atlaw, D., & Tariku, Z. (2021). Magnitude and factors associated with anemia among diabetic patients in Ethiopia: a systematic review and meta-analysis. SAGE Open Medicine, 9, 20503121211031126.https://doi.org/10.1177/20503121211031126

Bekele A, Teji Roba K, Egata G, Gebremichael B (2019) Anemia and associated factors among type-2 diabetes mellitus patients attending public hospitals in Harari Region, Eastern Ethiopia. PLoS ONE 14(12): e0225725. https://doi.org/10.1371/journal.pone.0225725

Bhatia, V., Chaudhuri, A., Tomar, R., Dhindsa, S., Ghanim, H., & Dandona, P. (2006). Low testosterone and high C-reactive protein concentrations predict low hematocrit in type 2 diabetes. Diabetes care, 29(10), 2289-2294.

Bolen S, Wilson L, Vassy J, et al. (2011). Comparative effectiveness and safety of oral diabetes medications for adults with type 2 diabetes. Agency for healthcare research and quality (US)

Christy, A. L., Manjrekar, P. A., Babu, R. P., Hegde, A., & Rukmini, M. S. (2014). Influence of iron deficiency anemia on hemoglobin A1c levels in diabetic individuals with controlled plasma glucose levels. Iranian biomedical journal, 18(2), 88.

Collins, A. J., Foley, R, N., Chavers, B. , Gilbertson, D., et. Al. (2012). 'United States Renal Data System 2011 Annual Data Report: Atlas of chronic kidney disease & end-stage renal disease in the United States. Am J

Kidney Dis. Jan;59(1 Suppl 1):A7, e1-420. doi: 10.1053/j.ajkd.2011.11.015. PMID: 22177944.

Craig, K. J., Williams, J. D., Riley, S. G., Smith, H., Owens, D. R., Worthing, D., ... & Phillips, A. O. (2005). Anemia and diabetes in the absence of nephropathy. Diabetes care, 28(5), 1118-1123.

Craig, K. J., Williams, J. D., Riley, S. G., Smith, H., Owens, D. R., Worthing, D., ... & Phillips, A. O. (2005). Anemia and diabetes in the absence of nephropathy. Diabetes care, 28(5), 1118-1123.

Dev, S., & Babitt, J. L. (2017). Overview of iron metabolism in health and disease. Hemodialysis International, 21, S6-S20. https://doi.org/10.1111/hdi.12542.

Flood, D., Seiglie, J. A., Dunn, M., Tschida, S., Theilmann, M., Marcus, M. E., ... & Manne-Goehler, J. (2021). The state of diabetes treatment coverage in 55 low-income and middle-income countries: a cross-sectional study of nationally representative, individual-level data in 680 102 adults. The Lancet Healthy Longevity, 2(6), e340-e351.

Goldhaber, A., Ness-Abramof, R., & Ellis, M. H. (2009). Prevalence of anemia among unselected adults with diabetes mellitus and normal serum creatinine levels. Endocrine Practice, 15(7), 714-719.

Hizomi Arani, R., Fakhri, F., Naeimi Tabiee, M., Talebi, F., Talebi, Z., Rashidi, N., & Zahedi, M. (2023). Prevalence of anemia and its associated factors among patients with type 2 diabetes mellitus in a referral diabetic clinic in the north of Iran. BMC Endocrine Disorders, 23(1), 1-8. Das, S. G., & Kumar, A. (2022). Anaemia and Its Associated Factors Among Type 2 Diabetes Mellitus Patients in Eastern India: A Cross Sectional Study. European Journal of Molecular & Clinical Medicine, 9(3), 5591-5598.

Ingternational Diabetes Federation (IDF) Diabetes Atlas. (2021). Diabetes around then world in 2021. https://diabetesatlas.org/#:~:text=Diabetes%20around%20the%20world%20in%202021%3A&text=Diabetes%20is%20responsible%20for%206.7,over%20the%20last%2015%20years.

Katroth, A., Narayanam, A., Chauhan, S., & Singh, A. (2018). Diabetes mellitus and metformin: fatal vitamin B12 deficiency associated with anemia and sepsis in a young adult. Journal of Applied Pharmaceutical Science, 8(3), 165-167.

Khatri, B. (2017, May). Study on Co-Morbidities In Patients With Type Ii Diabetes Mellitus. In Value In Health (Vol. 20, No. 5, pp. A163-A163). 360 Park Ave South, New York, NY 10010-1710 USA: Elsevier Science Inc.

Kim, M., Lee, S. H., Park, K. S., Kim, E. J., Yeo, S., & Ha, I. H. (2021). Association between diabetes mellitus and anemia among Korean adults according to sex: a cross-sectional analysis of data from the Korea National Health and Nutrition Examination Survey (2010–2016). BMC endocrine disorders, 21(1), 1-10.

Lin, X., Xu, Y., Pan, X., Xu, J., Ding, Y., Sun, X., ... & Shan, P. F. (2020). Global, regional, and national burden and trend of diabetes in 195 countries and territories: an analysis from 1990 to 2025. Scientific reports, 10(1), 1-11.https://doi.org/10.1038/s41598-020-71908-9

Marathias, K. P., Lambadiari, V. A., Markakis, K. P., Vlahakos, V. D., Bacharaki, D., Raptis, A. E., ... & Vlahakos, D. V. (2020). Competing effects of renin angiotensin system blockade and sodium-glucose cotransporter-2 inhibitors on erythropoietin secretion in diabetes. American Journal of Nephrology, 51(5), 349-356. Donate-Correa, J., Luis-Rodríguez, D., Martín-Núñez, E., Tagua, V. G., Hernández-Carballo, C., Ferri, C., ... & Navarro-González, J. F. (2020). Inflammatory targets in diabetic nephropathy. Journal of Clinical Medicine, 9(2), 458.

Mokgalaboni, K., & Phoswa, W. N. (2022). Cross-link between type 2 diabetes mellitus and iron deficiency anemia. A mini-review. Clinical Nutrition Open Science.

Nair, K. M., & Iyengar, V. (2009). Iron content, bioavailability & factors affecting iron status of Indians. Indian Journal of Medical Research, 130(5), 634-645.

Pan American Health Organization (PAHO). 2013. Half of people who have diabetes don't know it. On World Diabetes Day, PAHO/WHO recommends: "Know your risk and warning signs, get the care you need". Washington, D.C., 14 November 2013 (PAHO/WHO). https://www3.paho.org/hq/index.php?option=com_content&view=article&id=9157:2013-half-people-who-have-diabetes-dont-know-it&Itemid=0&lang=en#gsc.tab=0.

Radha, V., & Mohan, V. (2007). Genetic predisposition to type 2 diabetes among

Asian Indians. Indian Journal of Medical Research, 125(3), 259-274.

Ranil, P. K., Raman, R., Rachepalli, S. R., Pal, S. S., Kulothungan, V., Lakshmipathy, P., ... & Sharma, T. (2010). Anemia and diabetic retinopathy in type 2 diabetes mellitus. J Assoc Physicians India, 58(58), 91-94.

Roglic, G. (2016). WHO Global report on diabetes: A summary. International Journal of Noncommunicable Diseases, 1(1), 3.doi:10.4103/2468-8827.184853

Solomon D, Bekele K, Atlaw D, Mamo A, Gezahegn H, Regasa T, et al. (2022) Prevalence of anemia and associated factors among adult diabetic patients attending Bale zone hospitals, South-East Ethiopia. PLoS ONE 17(2): e0264007.https://doi.org/10.1371/journal.pone.0264007

Susan van, D., Beulens, J. W., Yvonne T. van der, S., Grobbee, D. E., & Nealb, B. (2010). The global burden of diabetes and its complications: an emerging pandemic. European Journal of Cardiovascular Prevention & Rehabilitation, 17(1_suppl), s3-s8.https://doi.org/10.1097/01.hjr.0000368191.86614.5a.

Tandon, N., Anjana, R. M., Mohan, V., Kaur, T., Afshin, A., Ong, K., ... & Dandona, L. (2018). The increasing burden of diabetes and variations among the states of India: the Global Burden of Disease Study 1990–2016. The Lancet Global Health, 6(12), e1352-e1362.

Vos, T., Abajobir, A. A., Abate, K. H., Abbafati, C., Abbas, K. M., Abd-Allah, F., ... & Criqui, M. H. (2017). Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. The Lancet, 390(10100), 1211-1259.

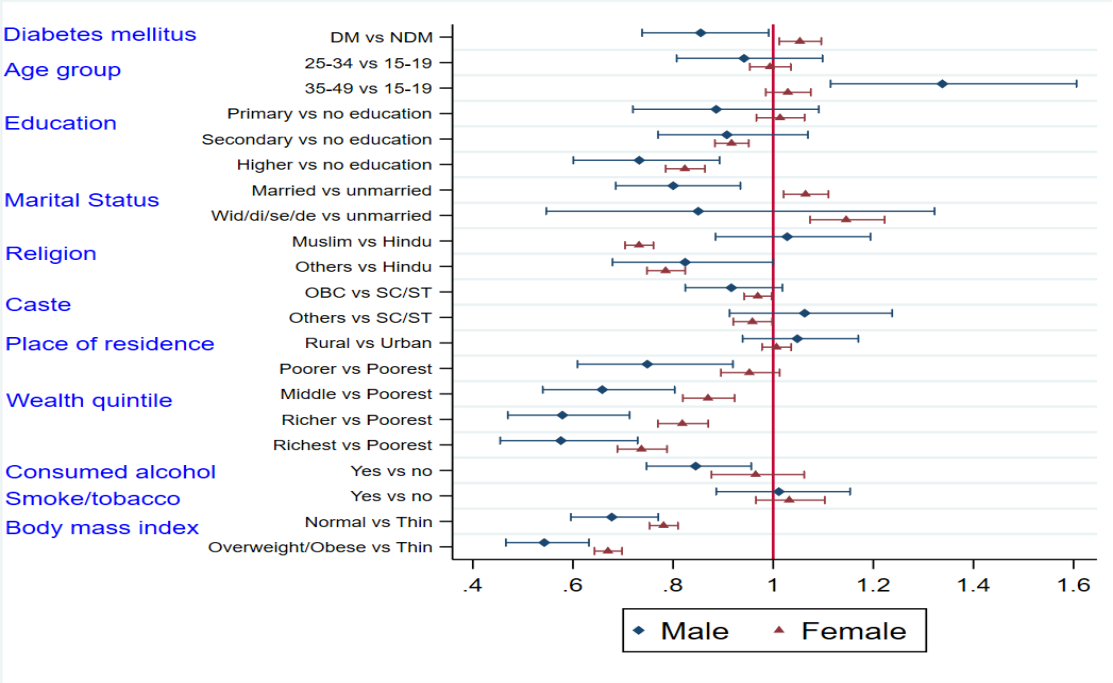
WorldHealth Organization. (2011). Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity (No. WHO/NMH/NHD/MNM/11.1). World Health Organization.

Wright, J. A., Oddy, M. J., & Richards, T. (2014). Presence and characterisation of anaemia in diabetic foot ulceration. Anemia, 2014.

Woodward M. Rationale and tutorial for analysing and reporting sex differences in cardiovascular associations. Heart. 2019;105:1701–8.

Zhang, X. X., Kong, J., & Yun, K. (2020). Prevalence of diabetic nephropathy among patients with type 2 diabetes mellitus in China: a meta-analysis of observational studies. Journal of diabetes research, 2020.Rizvi, N., & Nishtar, S. (2008). Pakistan's health policy: appropriateness and relevance to women's health needs. Health policy, 88(2-3), 269-281.

Figure S1 Sex specific odds ratios (RORs) for Anaemia associated with diabetes mellitus among adults aged 15-49 in Southern states of India, 2019-21



DM: diabetes mellitus; NDM: non-diabetes mellitus; Wid/se/di/de: widowed/divorced/separated/deserted