ABSTRACT

Title of Document: COMPARISONS OF WAIST CIRCUMFERENCE, WAIST-TO-HIP RATIO AND BODY MASS INDEX AND THEIR ASSOCIATIONS WITH TYPE 2 DIABETES IN RURAL AND URBAN INDIA.

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India has the highest prevalence of diabetes mellitus in the world. Anthropometric measurements (waist circumference (WC), waist-to-hip ratio (WHR) and body mass index (BMI)) are risk factors of Type 2 diabetes mellitus (T2DM). This study examined associations between these anthropometric measures and T2DM among 508 urban Indians in New Delhi and 574 rural Indians in Tamil Nadu. Using a receiver operator curve (ROC) the anthropometric cutpoints most strongly associated with T2DM were determined. Bivariate correlation and the area under the ROC curve showed most significant associations between T2DM and WHR (0.90 cm, 0.86; 0.87, 0.81 urban and rural men and women, respectively) followed by WC (86 cm, 85; 86, 75) and then BMI (24 kg/m^2, 21; 25, 22). Results from this study showed large variations in cutpoints between the rural and urban populations and suggest that no single cutpoint should be used in India due to large intra- and inter- regional differences within the country.

COMPARISON OF WAIST CIRCUMFERENCE, WAIST-TO-HIP RATIO, AND BODY MASS INDEX AND THEIR ASSOCIATIONS WITH TYPE 2 DIABETES IN RURAL AND URBAN INDIA

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By

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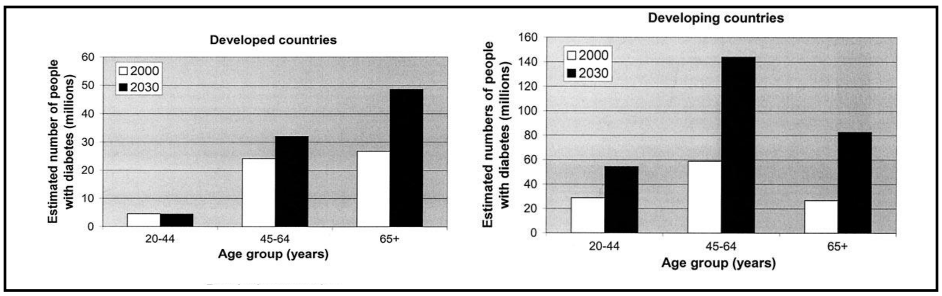
Chapter 1: Literature Review

The prevalence of Type 2 diabetes mellitus (T2DM) is increasing worldwide (Zimmet P). T2DM is an irreversible condition where the body no longer responds to insulin, thus preventing glucose from leaving the blood stream and entering the cells. T2DM is disproportionately affecting developing countries as illustrated in the graph below (Hossain, 2007).

Graph 1.1: Diabetes prevalence in developed and developing countries



India currently leads the world in diabetes cases, accounting for approximately 15% of the global diabetes burden with 61.3 million individuals diagnosed in 2011 (Sicree, Shaw, & Zimmet, 2006 and IDF, 2011). Studies have linked the high prevalence of diabetes in India to both genetic and lifestyle factors (Raghupathy, et al., 2007). Genetically, Asian Indians tend to have higher rates of insulin resistance, higher prevalence of low birth weight babies followed by catch up growth, higher levels of central adiposity, elevated low density lipoprotein (LDL) levels, serum triglyceride, and homocysteine levels and reduced high density lipoprotein (HDL) levels, as compared to Europeans and American Caucasians (James, Chen, & Inoue, 2002). All of these factors lead to an increased risk for Asian Indians to develop T2DM.

Section 1.1: Diabetes

In 1997 the World Health Organization (WHO) had a meeting to discuss the rising rate of obesity and its implications on public health. At this meeting, the health risks or co-morbidities associated with obesity were categorized into three different groups based on overall relative risk. As shown in Table 1, a relative risk of three indicates that the probability of developing the co-morbidities listed within column one are three times higher for obese individuals. T2DM falls within this category. Relative risk is defined as the ratio of the probability of the event occurring in the exposed group versus a non-exposed group (Garvan & Sistrom, 2004)

Table 1.1: Co-morbidities associated with Obesity (WHO, 1998)

Greatly increased (RR† >>3)	Moderately increased (RR 2-3)	Mildly increased (RR 1-2)
Type 2 diabetes	*Coronary heart disease*	*Cancer (breast cancer in postmenopausal women, endometrial cancer, colon cancer)*
Gallbladder diseases	*Hypertension*	
Dyslipidaemia	*Osteoarthritis (knees and hips)*	*Reproductive hormone abnormalities*
Metabolic Syndrome	*Hyperuricaemia and gout*	*Polycystic ovary syndrome*
Breathlessness		*Impaired fertility*
Sleep apnoea		*Low back pain*
		Increased anaesthetic risk
		Foetal defects associated with maternal obesity

†*Relative risks are approximate*

Diabetes currently affects 220 million people worldwide (WHO, 2009). The majority of these cases are T2DM, which affects 90-95% of the diabetic population (Ramachandran A. C., 2002). Since 1965, the WHO has published guidelines for the diagnosis and classification of diabetes. Diabetes is defined as a fasting plasma glucose level $\geq$ 7.0 mmol/l (126 mg/dl) or a 2 hour plasma glucose level $\geq$11.1mmol/l (200 mg/dl) (WHO/IDF, 2006).

The majority of individuals with diabetes are classified as either Type 1 or Type 2. Both Type I and Type II diabetes relate to the body's response to insulin. In a healthy individual, glucose levels rise after food is consumed. In response, the pancreas secretes insulin into the blood stream which acts as a key, allowing the glucose to enter the cells and lowering the glucose levels in the bloodstream. In Type 1 diabetes (T1D) insulin is not produced by the body and hence glucose and cannot enter the cells (WHO, November 2009). The causes of T1D are usually genetic or in response to destruction of beta cells as a result of exposure to certain viruses. Diagnosis of T1D usually occurs during childhood or adolescence.

In T2DM, the pancreas secretes insulin into the blood stream, but the insulin receptors on the cells have become resistant to the insulin and do not allow the glucose to enter the cells, resulting in elevated blood glucose levels (WHO, November 2009). T2DM is most often seen in older adults and is considered preventable. There is strong evidence that family history, race, and age increase an individual's likelihood of developing T2DM. The causes of T2DM have been linked to obesity, physical inactivity, gestational diabetes, insulin resistance, impaired glucose tolerance (IGT) and impaired fasting glucose (IFG).

Insulin resistance occurs when an individual produces insulin but the receptors that allow the glucose into the cells have become semi- resistant and elevated levels of insulin are seen in the blood stream. IGT and IFG occur after prolonged periods of insulin resistance and are defined by blood sugar level being above the normal but not high enough to be classified as T2DM. IGT is classified as 2-hour glucose levels of 140 to 199 mg per dL (7.8 to 11.0 mmol/L)(WHO/IDF, 2006). IFG is defined as fasting plasma glucose values of 100 to 125 mg/dL (5.6 to 6.9 mmol/L). Normal fasting plasma glucose values should be below 100 mg/dL (Rao, 2004). Patients with IFG or IGT are at significant risk of developing diabetes (Rao, 2004). Nearly one third of the IGT population will eventually develop diabetes (Alberti , 1996).

T2DM has both long and short term complications. The short term complications develop quickly and require immediate attention. Complications include ketones in the urine, high blood sugar (hyperglycemia) and low blood sugar (hypoglycemia) (IDF, 2011).   In T2DM, because the body no longer responds normally to insulin, there is large variation in blood sugar levels. Some examples of actions that can result in fluctuations of blood glucose levels include dietary intake of carbohydrates and alcohol resulting in high blood sugar, while taking cold medicine with diabetes medication and vigorous exercise can cause low blood sugar.

Long term complications associated with diabetes develop gradually. These include heart and blood vessel disease, nerve damage (neuropathy), kidney damage (nephropathy), eye damage (retinopathy), and foot damage (IDF, 2011)). Nearly 75% of people with diabetes die of some type of heart or blood vessel disease as a result of clogged arteries (WHO, November 2009).

Studies have shown that the strongest contributors to T2DM are preventable lifestyle factors: obesity and inactivity (Lev-Ran, 2001). There have been several conflicting studies about the importance of waist circumference (WC) and waist-to-hip ratio (WHR), both measures of centralized obesity, as compared to body mass index (BMI), a measure of generalized obesity as methods for identifying risk for developing T2DM (Pua, 2005; Deepa, 2009, Snehalatha, 2003). In 2009, a cross-sectional review of 52 studies examining WC and BMI as predictive tools for diabetes found that neither WC nor BMI showed a stronger link to diabetes, but that both are useful tools for predicting risk (Qiao, 2009).

Section1.2: Anthropometric Measures

Subsection 1.2.1: WHO Cutpoints

The rapid increase of diabetes worldwide has necessitated the need for finding a low cost solution which identifies risk factors and provides early lifestyle interventions to help prevent future T2DM cases (Qiao, 2009). There are several strategies for preventing the development of T2DM; these include diabetes education (which teach strategies for managing weight and physical activity), maintaining a healthy body weight, eating a low fat diet, staying physically active and early and frequent screening for diabetes. Several programs have recommended using the WHO's BMI and WC cutpoints as guidelines for individuals to maintain a healthy weight, define abdominal and centralized obesity, and understand the risks of co-morbidities as defined in Table 1 at increased BMI and WC levels (Rolka, 2001; Lindstrom, 2003; Schulze, 2007).

BMI is the ratio of an individual's weight in kilograms divided by their height in meters squared (kg/m^2). It is considered a measure of generalized obesity. WC is a measure of abdominal or centralized obesity, and is taken by measuring the smallest horizontal girth between the costal margins and the iliac crests in centimeters.

In the WHO's June 1997 report titled, *Obesity: Preventing and Managing a Global Epidemic*, which defined BMI and WC cutpoints, WC is shown to provide a more practical correlate for abdominal obesity and associated co-morbidities as compared to WHR. The report also identifies WHR as a useful research tool which provides additional information about gluteofemoral muscle mass and bone structure. The WHO did not make an official recommendation for appropriate WHR cutpoints in this report, but did cite previously accepted guidelines for WHR; specifically WHR >1.0 in men and WHR >0.85 in women. (WHO, 1997)

However, several researchers consider WHR as a better tool to more accurately assess abdominal obesity because it accounts for overall body size. This reduces the risk of misclassifying someone who is tall from being abdominally obese (Seidell, 2001). Studies in 2004 and 2006 by Yajnik have shown significant association between WHR and hyperglycemia. Research by Deepa et al postulates that increases in WHR also suggest an increase in the Thrifty phenotype, which has been linked to increases in T2DM (Deepa, 2009).

Table 1.2 shows the BMI and WC cutpoints in relation to their relative risk of co-morbidities that were defined in the WHO 1997 report on obesity. The list of co-morbidities associated with obesity is shown in Table 1.1 (WHO, 1997). These cutpoints are not country specific.

Table 1.2: WHO 1997 Co-morbidities risk associated with different values of Body Mass Index (kg/m^2) and suggested Waist Circumference (cm) cutpoints

Classification	**BMI (kg/m^2)**	**Risk of Co-morbidities**
Underweight	< 18.5	Low
Normal Weight	18.5-24.9	Average
Overweight	$\geq$ 25	
Pre Obese	25-29	Increased
Obese I	30-34.9	Moderate
Obese II	35-39.9	Severe
Obese III	$\geq$ 40	Very severe
Abdominal obesity WC: $\geq$ 94 cm in men and $\geq$ 80 cm in women		

A BMI below 25 kg/m^2 and a WC below 94 cm in men and 80 cm in women is considered healthy, with an average risk of co-morbidities.

Subsection 1.2.2: WHO Asian Specific Cutpoints

Since the cutpoints were first published in 1993 and reaffirmed in the 1997 Obesity Report by the WHO, there has been an increased reporting of T2DM and other cardiovascular risk factors in Asian populations that are within normal BMI and WC values (BMI$\geq$ 25 kg/m^2 and WC $\geq$ 90 cm men and WC $\geq$ 80 cm women).

Based on the result of these reports, there have been three WHO meetings to explore the need for developing Asian specific BMI and WC cutpoints. Studies have shown that Asian populations tend to have smaller bone structure, higher body fat percentages for a specific BMI, and greater centralized obesity as compared to American or European populations (A Misra, 2004). In 2000, Asian specific cutpoints were defined as BMI greater than 23 kg/m^2 as overweight, and WC of greater than 90 cm in men and 80 cm in women as abdominally obese. Although, WHR was discussed in this report, an Asian-specific WHR was not provided because it stated that WC is the preferred measure of abdominal obesity. Table 1.3 summarizes the Asian specific cutpoints defined at that meeting. (WHO/IASO/IOTF, 2000)

Table 1.3: WHO 2000 Body Mass Index (kg/m^2) and Waist Circumference (cm) cutpoints in Adult Asians and their relation to co-morbidity risk

Classification	**BMI (kg/m^2)**	**Risk of Co-morbidities**
Underweight	< 18.5	Low
Normal Weight	18.5-22.9	Average
Overweight	$\geq$ 23	
Pre Obese	23-24.9	Increased
Obese I	25-29.9	Moderate
Obese II	$\geq$ 30	Severe
Abdominal obesity: WC: $\geq$ 90 cm in men and $\geq$ 80 cm in women		
*No WHR given. Report state WC is preferred measure of abdominal obesity		

In 2002, the WHO committee met on July 8-11, 2002 in Singapore to discuss the Asian specific cutpoints. It was determined that because the term Asian covers a broad spectrum of people, characteristics, cultures, degrees of urbanization, economic conditions and nutrition transitions, currently available Asia-specific data does not indicate a clear BMI cutpoint for the entire Asian population. Current data shows that co-morbidity risk varies from cutpoints 22-32 kg/m^2 between different Asian populations. Based on these results, it was decided that BMI cutpoints for Asian populations should be country specific, and based on valid and reliable measurements made in clinical settings (Consultation, 2004).

Section 1.3: India's Diabetes Epidemic

India leads the world in diabetes cases with 61.3 million individuals affected in 2011. (IDF, 2011) The diabetes burden accounted for $2.2 billion in annual health care costs to India in 2007 (Siegel, 2008). In contrast to developed countries, Asian Indians are being diagnosed with T2DM at a much younger age. A study in India showed 54.1% of diabetes cases were diagnosed before the age of 50 years. In developed countries, the majority of T2DM cases are diagnosed after the age of 65 years(Wild, 2004; Mohan, 2007). The earlier age of onset of diabetes in India increases the chances of individuals developing chronic complications of diabetes later in life, and results in a greater cost to the Asian Indian economy. The high prevalence of diabetes within India can be attributed to both lifestyle and genetic factors.

Subsection 1.3.1: India by Region

India is a country with vast regional variations in diet, lifestyle, urbanization and diabetes prevalence. However, there are currently limited studies on nationwide trends related to T2DM. Instead, most studies focus on one general area within India.

In a study conducted between 2003 and 2005, researchers looked at the prevalence of self-reported diabetes in both rural and urban India. The study looked at six different geographical locations in India (East, South, 2 from the North, West, and Central India). Results showed that for all regions, T2DM is directly related to wealth and urbanization. The association of wealth and diabetes in India is in contrast to western countries where diabetes is higher among lower economic groups (Mohan, 2008). The results of this study are summarized in Table 1.4. Specifically, the study shows that the overall prevalence of self reported diabetes is 7.3% in urban areas, 3.2% in peri-urban/ slums, and 3.1% in rural areas.

Table 1.4: Center-wide prevalence of self reported diabetes (Mohan, 2008)

Regions	Places	Prevalence of self-reported diabetes (%)			
		Rural (n = 13,522)	Peri-urban/slum (n = 15,751)	Urban (n = 15,230)	Overall (n = 44,503)
North India	Delhi (n = 5103)	–	1.8	$10.3^{\#}$	6.0
	Ballabgarh (n = 7990)	1.1	2.3^{*}	$4.8^{*,\#}$	2.7
South India	Chennai (n = 7847)	3.9	6.6^{*}	$8.7^{*,\#\#}$	6.4
	Trivandrum (n = 7537)	9.6	6.6^{*}	$11.2^{**,\#}$	9.2
East India	Dibrugarh (n = 8365)	0.6	1.4^{**}	$5.5^{*,\#}$	2.4
West/Central India	Nagpur (n = 7661)	0.6	0.6	$3.2^{*,\#}$	1.5
Overall	(n = 44,503)	3.1	3.2	$7.3^{*,\#}$	4.5

$^{*}p < 0.001$ and $^{**}p < 0.05$ compared to subjects in rural area. $^{\#}p < 0.001$ and $^{\#\#}p < 0.05$ compared to subjects in peri-urban/slum area.

Since earlier studies have shown that for every known case of diabetes, there is at least one unknown case, the overall total diabetes prevalence from this study is hypothesized to be 14.6% urban, 6.4% peri-urban, and 6.2% in rural. These predicted values correlate closely to overall diabetes prevalence reported in Chennai in 2004, with a prevalence of 15.5% in Chennai for the urban population, and 2.7% in rural areas using WHO data (Mohan, 2008).

These results show that overall diabetes prevalence varies greatly both within and between regions (Mohan, 2008). However, all diabetes cases were self reported in the study by Mohan et al 2008 and general knowledge of diabetes within those who participated was very low. General T2DM knowledge in India will be discussed in greater detail in section 4 of this chapter.

Within India, there is very limited data on the rural Indian population and T2DM prevalence. One study found that despite lower levels of T2DM in rural areas as compared to urban areas, impaired glucose tolerance levels within rural areas were still high (Ramachandran, 1992). Based on these results, the study suggests there may be genetic factors making Asian Indians more susceptible to T2DM.

Subsection1.3. 2: Lifestyle and Genetic factors related to T2DM in India

The major risk factors associated with T2DM in India are similar to developed countries: obesity and physical inactivity. In contrast to developed countries, the prevalence of diabetes is higher in urban areas and is considered a disease of affluence; whereas in developed countries T2DM is more often seen in lower socioeconomic groups (McDermott, 2000; Mohan, 2008). Researchers hypothesize that rapid urbanization and nutrition transition within India can be used to explain this trend. Over the past three decades, there has been rapid urbanization within India (Dech, 2009). Several trends have been noted among Asian Indians moving from a rural to urban location. These include an intake of excess calories, reduction in complex carbohydrates, increase in consumption of simple sugars and fats, and a decrease in activity level as a result of more sedentary jobs (Siegel, Naraya, & Kinra, 2008). Food balance data from the Food and Agriculture Organization in 2011 have shown small changes in energy intake but large changes in the types of foods consumed for energy. Specifically, there has been a shift towards increased consumption of animal products, sugars and fats, with the overall net effect being a shift to increased fat intake each year (Shetty, 2002).

In addition to lifestyle factors, there is increasing evidence that there are genetic factors that make Asian Indians more susceptible to T2DM (Ramachandran, 1992). In India, nearly 75% of T2DM patients have a first degree family history of diabetes (i.e. immediate family member who has diabetes) which indicates a genetic predisposition to diabetes among Asian Indians (Viswanathan, 1996). Asian Indians have higher insulin resistance and abdominal obesity than white Europeans with the same BMI (Misra, 2004). Within India, insulin resistance has been shown to be adversely affected by small increases in BMI. Furthermore, Asian Indians tend to have low birth weight babies that are then followed by catch-up growth (Misra, 2004) and India accounts for nearly 40% of the worlds burden for low birth weight babies with 7.4 million in 2009 (UNICEF, 2011). This trend has been linked to insulin resistance in adult-hood, and may partially explain why Asian Indians are more insulin resistant than other populations (Wilkin, 2002).

The high prevalence of diabetes among Asians Indians has resulted in the development of the Asian Indian Phenotype Hypothesis (Joshi, 2003). This term refers to the genetic predisposition of Asian Indians to a variety of diabetes risk factors. Risk factors include increased waist circumference and lower levels of obesity compared to other ethnic groups at lower levels of obesity, increased visceral fat, increased body fat from birth as compared to their Caucasian counterparts, higher degree of insulin resistance, and evidence of hyperinsulinemia. Additional studies have shown that Asian Indians tend to have low levels of adiponectin when compared to Caucasian counterparts (Mohan & Deepa, 2006). Adiponectin is a cytokine released from adipose tissue that protects against diabetes, and has several metabolic functions including regulation of energy homeostasis, decreasing plasma glucose, increasing clearance of glucose load, and decreasing insulin resistance.

Research suggests that central obesity, measured by WC or waist-to-hip ratio (WHR), is a stronger risk indicator of insulin resistance and T2DM than generalized obesity as measured by BMI (Kumar, 2006). Asian Indian women tend to have greater levels of centralized obesity, despite low levels of overall obesity compared to American and European Caucasians, which may contribute to the higher incidence of T2DM among women in India (Ramachandran, 2002). All of these factors contribute to the hypothesis that Asian Indians may be more predisposed to diabetes than other populations.

<u>Section 1.4: Diabetes knowledge in India</u>

Within India, there is a lack of understanding and knowledge about the causes, effects, and prevention of diabetes. In a cross sectional study in Chennai, India, a questionnaire shown in figure 1.1 was given by trained professionals to study participants to assess diabetes knowledge among the urban populations. (Deepa, 2005)

Figure 1.1: Diabetes Questionnaire: Chennai

Questions

1. Do you know what diabetes is?
   Yes ☐ No ☐
2. Do you think, in general, more and more people are getting affected with with diabetes nowadays?
   Yes ☐ No ☐ Don't know ☐
3. What are the factors you think that contribute to diabetes?
   a. Obesity ☐ b. Decreased physical activity ☐
   c. Family history of diabetes ☐ d. Mental stress ☐
   e. Consuming more sweets ☐
   f. Others (name)__________
4. Do you know that diabetes can cause complications in other organs?
   Yes ☐ No ☐ Don't know ☐
   a) If yes, what are they?
   1.______ 2.______ 3.______ 4.______
5. Can diabetes be prevented?
   Yes ☐ No ☐ Don't know ☐

Of the 26,001 individuals surveyed, only 75.5% of the sample was aware of a condition called diabetes, 22.2% of the entire sample and 41.0% of the self reported diabetic sample knew that diabetes could be prevented. An understanding of the complications and causes of diabetes was also very limited; 19.0% of the entire sample population was aware that diabetes could cause complications and only 11.9% of the sample was aware that obesity and physical inactivity could increase the risk of diabetes. (Deepa, 2005) Analysis from this study demonstrates the need for diabetes education programs in India to help with diabetes prevention.

Section 1.5: Indian Specific BMI and WC Cutpoints to prevent T2DM

A study conducted in Chennai addressed specific BMI and WC cutpoints and their association with metabolic risk and diabetes prevalence (Deepa, 2009). Obesity and WC were defined using WHO Asia specific criteria (Table 1.3). BMI cutpoints were examined at 23, 25, 27.5 and 30. General characteristics of the study population are shown in the table 1.5. This study shows men have a higher WC, WHR, fasting plasma glucose, and higher prevalence of diabetes when compared to women. Women had higher BMI and hip circumference as compared to men ($p<0.05$). There was no significant difference in the IGT prevalence.

Table 1.5: General Characteristics of Study Population (Deepa, 2009)

Variables	Men (n = 1096)	Women (n = 1254)	P-value
Age (years)	41 ± 14	38 ± 12	<0.001
Education			
Illiterate (%)	6.0	18.2	
Some schooling (%)	76.0	72.7	
Graduate and above (%)	18.0	9.1	
Body mass index (kg m^{-2})	22.6 ± 3.8	23.1 ± 4.1	<0.05
Waist circumference (cm)	85.3 ± 11.6	81.7 ± 11.2	<0.001
Hip circumference (cm)	91.5 ± 8.0	95.6 ± 9.2	<0.001
Waist-to-hip ratio	0.93 ± 0.09	0.85 ± 0.08	<0.001
Systolic blood pressure (mm Hg)	121 ± 18	117 ± 18	<0.001
Diastolic blood pressure (mm Hg)	76 ± 11	73 ± 11	<0.001
Fasting plasma glucose (mg dl^{-1})	99 ± 38	94 ± 36	<0.05
Total cholesterol (mg dl^{-1})	179 ± 39	180 ± 38	0.352
Triglycerides (mg dl^{-1})	138 ± 96	114 ± 70	<0.001
HDL cholesterol (mg dl^{-1})	40 ± 9	45 ± 10	<0.001
HbA1C (%)	6.2 ± 1.5 (min: 3.6, max: 14.6)	5.9 ± 1.3 (min: 3.1, max: 16.6)	<0.001
Diabetes (%)	18.0	13.4	<0.05
Impaired glucose tolerance (%)	10.3	10.8	0.720

Abbreviations: HbA1c, glycated hemoglobin; HDL, high-density lipoprotein.

The percent of the population considered obese based on the four BMI cutpoints in the study are detailed in Table 1.6. There is a significant increase in obesity prevalence when the cutpoint is adjusted from the standard BMI cutpoint of 25 kg/m^2 to the Asian specific cutpoint of 23 kg/ m^2; 26.5% to 45.9% respectively.

Table 1.6: Percent of population considered obese by defined cutpoint (Deepa, 2009)

BMI Cutpoint	Percent of Population Considered Obese
≥ 23 kg/m^2	45.9%
≥ 25 kg/m^2	26.5%
≥ 27.5 kg/m^2	9.9%
≥ 30 kg/m^2	4.0%

The age standardized prevalence of abdominal obesity was 46.6%. Final results showed that WC and WHR are better predictors of obesity related diabetes among Asian Indian women when compared to BMI using the Asian specific cutpoints defined in Table 1.3 (Deepa, 2009). Results from this study affirm that there should be separate BMI and WC cutpoints for the Asian Indian population.

A second study was performed in 6 different regions in India, with 10,025 adults over the age of 20, to determine BMI and WC cutpoints for India using Indian specific data (Snehalatha, 2003). Instead of defining specific cutpoints, this study looked at significant association between T2DM and BMI and T2DM and WC and plotted them on a receiver operator characteristic (ROC) curve. The point on the ROC curve that corresponds to the largest area is taken to be the ideal cutpoint. The mean BMI and WC for men were 22.4 ± 4.2 kg/m^2 (mean and standard deviation) and 80.7 ± 12.2 cm respectively. For women the mean BMI and WC was 23.6 ± 4.9 kg/m^2 and 79 ± 13 cm respectively. The odds ratio between diabetes in men and women and BMI were shown to be significant at the categories of 23-24 kg/m^2 (P = 0.0045, OR 2.27, 95% CI 1.29-3.99 for men; P = 0.009, 2.03, 1.19-3.46 for women). The optimum cutpoints obtained from the ROC curve were found to be a BMI of 23 kg/m^2 and a WC of 85 cm in men and 80 cm in women. The author proposed a new WC cutpoint of 85 cm for men which are much lower than the WHO defined Asian specific cutpoints of 90 cm, based on the strong association found between these suggested values (85 cm) and T2DM. The BMI cutpoint and WC for women found in this study agrees with the current Asian specific WHO cutpoint (23 kg/m^2 and 80 cm)

Section 1.6: Summary

India is the diabetic capital of the world with 60.3 million diagnosed in 2011. WC, WHR, and BMI cutpoints offer a simple and inexpensive assessment of T2DM risk. Current cutpoints as defined by the WHO in 1998 are not representative of Asian populations. Asian Indian specific cutpoints need to be defined for India, because of the large variations in body composition within Asian populations. In the present study, we will look at associations between central obesity (WC and WHR) and generalized obesity (BMI) and their associations with T2DM to determine Asian Indian-specific cutpoints.

There is currently very limited data on rural Indian populations and rural/urban populations. A comparison of urban and rural Indians' T2DM risk factors can provide a better understanding of the general characteristic trends and differences between these two groups. Hence the purpose of this study was to determine which anthropometric measurement, BMI, WC or WHR is more strongly associated with T2DM and IFG to define recommended cutpoints in rural and urban Indians. Currently, there is very limited data that looks at all three measures of obesity and their relationship to type T2DM and IFG.

The results from the present study will help to better understand the T2DM and IFG rates in the rural and urban Indian subpopulations for Tamil Nadu (rural) and New Delhi (urban). The results from this study cannot be generalized to all Asian Indians because there is a large genetic variation among individuals in India across the different states as well as intra-regional differences.

Chapter 3: Research Questions

1. What is the optimal BMI cutpoint for predicting diabetes in Asian Indians?
    a. We will analyze the data of men and women and rural and urban populations separately. If a significant association between BMI and T2DM is found, a ROC curve will be generated from the data to determine the optimal cutpoint.
2. What is the optimal WC cutpoint for predicting diabetes in Asian Indians?
    a. We will analyze the data of men and women and rural and urban populations separately. If a significant association between WC and T2DM is found, a ROC curve will be generated from the data to determine the optimal cutpoint.
3. What is the optimal WHR cutpoint for predicting diabetes in Asian Indians?
    a. We will analyze the data of men and women and rural and urban populations separately. If a significant association between WHR and T2DM is found, a ROC curve will be generated from the data to determine the optimal cutpoint.
4. Are there differences between rural and urban Asian Indian populations with regards to diabetes prevalence and IFG?
5. What anthropometric indicator, BMI, WC, or WHR, is more strongly associated with T2DM in Asian Indians?
    a. Which measure of centralized obesity (WC or WHR) is more strongly associated with T2DM?

Chapter 4: Methods

Section 4.1: Background Overall Study

The data for this research is taken from a larger study of rural and urban Asian Indian institutions that participated in the study titled, "Population Based Study of Diabetes and Metabolic Correlates of Cardiovascular risk factors among Asian Indians." The study design was comprised of a multicenter, cross-cultural, epidemiological study involving several US and two Indian institutions. The sample in India was composed of urban and rural Indians eighteen years and older. This study started in 2005, and was completed in 2007 (Misra, 2010). Our study will only analyze the data gathered in New Delhi and Tamil Nadu India.

Section 4. 2: India Urban and Rural Sample Population

The two samples from India came from two different locations; one urban and one rural. The urban Indian population sampled 508 individuals from New Delhi located in North West India. The rural population sampled 574 individuals from Aalamarathupatti village in Tamil Nadu located in Southern India.

Figure 4.1 Map of India (http://www.nationsonline.org/oneworld/india_map.html)

The urban Indian population in New Delhi was selected based on the WHO multi-stage cluster sampling technique to randomly select individuals from the urban site as described below. A list of all the residential colonies within ten kilometers of the All India Institute of Medical Sciences (AIIMs) was prepared. Colonies were randomly selected to and a list of the number of total households in each colony was prepared. Specific households were randomly chosen, and one member from each chosen house was invited to take part in the study. The Resident Welfare Associations from each selected colony was responsible for validating the list. Data was collected by trained investigators from AIIM. The Resident Welfare Association represents the interest of citizens or people living in a specific urban or suburban locality.

Nine hundred urban respondents were invited to participate in the study. These study participants represented a wide range of socio-economic strata. Out of the 900 participants, 610 (response rate 67.7%) individuals completed the face-to-face interviews with trained data collection staff. The questionnaire used in the interviews was prepared in both Hindi and English and was pre-tested and validated in each selected colony on a smaller sample (N=10). Five hundred and eight (response rate of 56.4%) selected individuals completed anthropometric measurements, and provided venous blood samples after an overnight fast of at least 8 hours. The most common reason for the New Delhi individuals to refuse to participate in the study was that they did not want to take time off of work for the survey and complete the blood work.

The procedure for selecting the rural study participants was to first use government land records which identified hamlets classified as rural. Of the thirty rural hamlets identified through the government records, eight were randomly selected to participate in the rural population study. In door-to-door visitations, 850 individuals were contacted and 599 rural Indians (response rate 70.4%) agreed to participate in the face-to-face interviews by trained interviewers. Anthropometric measurements and fasting blood work was completed by 574 of the 850 individuals (response rate of 67.5%) at the Gandhigram Rural Institute. The majority of the respondents that refused to participate in the rural study were migrant workers that were unable to take time off work.

Subsection 4.2.1: Data Methods

The study was approved by the Institutional Review Board of Texas A&M University and the All India Institute of Medical Sciences (AIIMS). AIIMS served as the core laboratory for biochemical analysis for the urban and rural Indian population.

Information gathered on each participant included demographic profile such as age, gender, marital status, anthropometrics, T2DMM and CVD risk factors e.g., blood pressure, smoking, monthly income, fasting blood glucose values, serum lipids, fasting plasma insulin, and education. The primary endpoint, or main focus, of the study was the prevalence of diabetes, metabolic syndrome (MetS), and CVD risk.

Subsection 4.2.2: Anthropometric Measurements

Field staff taking the anthropometric measurements participated in a workshop prior to the data collection for standardized and culturally appropriate method for taking the measurements. Measurements were taken by one member of the field staff while another member of the staff served as an observer for men and women. The intra- and inter- observer variation was less than 10%. The study protocol and data collection procedures were standardized using calibrated equipment at both the rural and urban locations. All research assistants were trained at AIIMs and were monitored during the study period. The anthropometric measurements taken by the staff included height, weight, waist circumference, and hip circumference. Height was measured to the nearest centimeter using non-flexible measuring tape. Each subject was asked to stand upright without shoes against the wall with eyes directed forward and heels together. The distance from the floor to the highest position of the head was measured to indicate the subject’s height. Weight was measured using a spring balance on a firm level surface. Subjects wore light clothing and no shoes. Subjects stood upright with their weight evenly distributed on both feet and looked straight ahead. Weight was recorded to the nearest kilogram. Body mass index was calculated as weight in kilograms divided by height in meters squared (weight (kg)/ height (m^2)). Waist circumference was taken using a non-elastic measuring tape. Subjects stood erect in a relaxed position with both feet together on a level surface. WC was measured as smallest horizontal girth between the costal margins and the iliac crests at minimal respiration. Two measurements were taken, and the mean was rendered as the WC in centimeters. Hip circumference (HC) was measured with a non-elastic measuring tape positioned around the hips at the level of the symphysis pubis and the greatest gluteal protuberance. Two measurements were taken, and the mean was rendered as the HC in centimeters. Waist-to-hip ratio was calculated as the WC (cm) divided by HC (cm) (WC/HC).

Subsection 4.2.3: Biochemical Measures

A venous blood sample was obtained after an overnight fast of at least 8 hours for fasting plasma glucose (FPG). The serum levels of total cholesterol, triglycerides, fasting blood glucose and HDL-c were measured using commercially available reagent kits (Randox Laboratory, San Francisco, CA, USA) on a semi-automated analyzer (das srl, palombara, Sabina, Italy). Value of LDL-c was calculated using the Friedewald's equation.

Subsection .4.2.4: Demographic Characteristics

As part of the questionnaire, general demographic characteristics were gathered from the urban and rural sample population. Tobacco use was characterized by never, sometimes, regularly and stopped more than six months ago. Tobacco use included cigarettes, tobacco, and cigars. Education level was also assessed based on the highest level achieved by the study participant and included; never attended, elementary (grades 1-8), matriculation (grades 9-10), high school (grades 11-12), some college or diploma, graduate school, and post graduate or professional school. Financial data on the each group was assessed using the following cutpoints, <500 rupees (Rs), 501-1500 Rs, 1501-2500 Rs, 2501-3500 Rs, 3500-5000 Rs, 5001-10000Rs, and >10000 Rs. 500 Rs is roughly equivalent to 10 US dollars.

Subsection 4.2.5: Classifications

Overweight and obesity were determined using the WHO Asian specific cutpoints; BMI $\geq$ 23 kg/m^2 and $\geq$ 25 kg/m^2 respectively based on the WHO Asian specific cutpoints. Abdominal obesity was defined using the cut-off points of waist circumference (WC), $\leq$ 90 cm in men and $\leq$ 80 cm in women, as defined by NCEP, ATP III and WHO Asian specific cut-off points. Diabetes was defined as FPG $\geq$ 126 mg/dL and/or a self-reported admission to the question "Have you ever been told by a doctor or health professional that you have diabetes or are on treatment for diabetes." Hypertension was defined as blood pressure $\geq$ 140/90 mm Hg and/or self-reported admission for the question "Have you ever been told by a doctor or health professional that you have hypertension or high blood pressure?" Family history of diabetes was defined as one immediate family member, parent or grandparent being diagnosed with diabetes. Tobacco use was assessed using responses from the survey which asked individuals about their average use of tobacco in any form. All data from this study was entered into the statistical analysis program SPSS.

Section 4.3: Statistical Analysis

Associations between BMI, WC and T2DM were conducted using the statistical software in SPSS. Data was stratified by location (urban or rural) and gender (men or women) A histogram showing the overall spread of BMI and WC for each group was plotted and average BMI and WC values were listed and compared. Individuals in each subpopulation were classified according to their diabetes status as normal, IFG, or T2DM. The percentage of diabetes cases within specified BMI and WC ranges was calculated for each group.

Significant association between diabetes and BMI, WC and WHR was verified prior to multinomial logistic regression analysis. Statistical significance was defined as association of the null hypothesis of less than 0.01.

The Pearson Correlation coefficient (r) was used to examine associations between T2DM and BMI, WC and WHR.

To determine recommended cutpoints for BMI, WC and WHR Receiver Operator Characteristic (ROC) curves with 95% confidence intervals were determined. The ROC curves provide a graphical representation of the tradeoff between the false negative (individuals with diabetes below the cutpoint) and false positive rates (individuals without diabetes above the cutpoint) for every possible cut off value (Zweig & Campbell, 1993). This method gives the ability to optimize both sensitivity and specificity in choosing recommended cutpoints. The sensitivity of the ROC curve is defined as the proportion of individuals who are diabetic and were identified correctly according to specific anthropometric cutpoints. The specificity is a measure of the proportion of individuals who do not have diabetes and were identified correctly. The ideal cutpoints for each population are determined by finding the point on the ROC curve that corresponds to the largest area.

Chapter 5: Results

Generalized characteristics for the study population are shown in Table 5.1.

Table 5.1: General Characteristics of Population

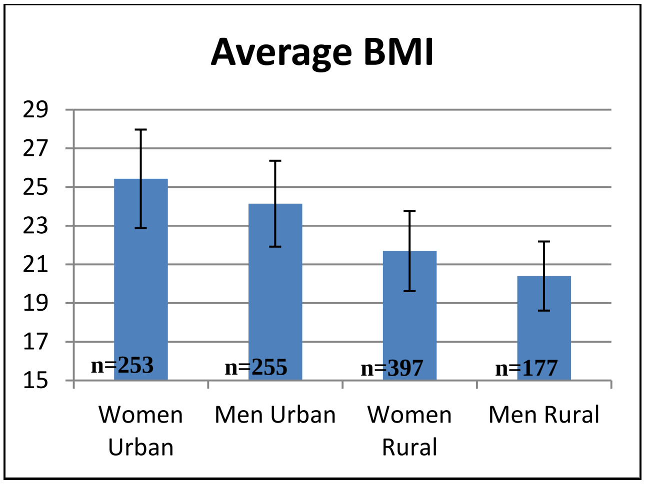
	Urban Sample Population		**Rural Sample Population**	
Variables	Men (N=255)	Women (N=253)	Men (N=177)	Women (N=397)
Age	43 ± 12.8	42 ± 10.7	41 ± 154	39 ± 13.6
BMI (Kg/m^2)	24.1 ± 4.4	25.4 ± 5.1	20.4 ± 3.6	21.7 ± 4.1
WC (cm)	90.1 ± 13	89.1 ± 13.2	78.8 ± 11.7	72.9 ± 10.8
Hip circumference (cm)	93.2 ± 8.1	97.2 ± 9.4	87.3 ± 7.7	89.0 ± 9.1
Waist-to-Hip Ratio	0.96 ± 0.08	0.92 ± 0.09	0.90 ± 0.07	0.82 ± 0.08
Systolic BP (mm HG)	123 ± 18	123 ± 20	115 ± 17	115 ± 19
Diastolic BP (mm Hg)	83 ± 10	81 ± 11	73 ± 11	72 ± 10
% Diabetes (FPG≥7.0mmol/l)	13.3	13.8	10.2	7.6
% IFG (5.6 ≤FPG≤7.0mmol/l)	25.9	17.8	13.6	12
%Normal (FPG≤5.5 mmol/l)	60.8	68.4	76.1	80.4
% Family history with T2DM	21.2	13	16.9	22.4
% Use tobacco	29	16.2	31.1	24.7
Education Completed				
% No school	18.8	30.8	24.9	21.2
% Elementary	18.8	19.8	36.7	42.3
% Middle	10.6	8.3	20.9	22.4
% High	11.4	8.7	5.1	6.3
% College or higher	40.4	41.1	12.4	7.8
Monthly Income *				
% < Rs 500	.4	.4	5.7	5.8
% Rs501 - 1500	.8	.8	46.3	55.9
% Rs1501 - 2500	1.6	2.0	21.5	18.1
% Rs 2501 - 3500	7.8	4.0	9.0	8.1
% Rs. 3501 - 5000	6.7	9.1	14.1	9.3
% Rs 5001 - 10,000	24.7	34.0	3.4	2.5
% > Rs 10,000	58.0	49.8	0	.3

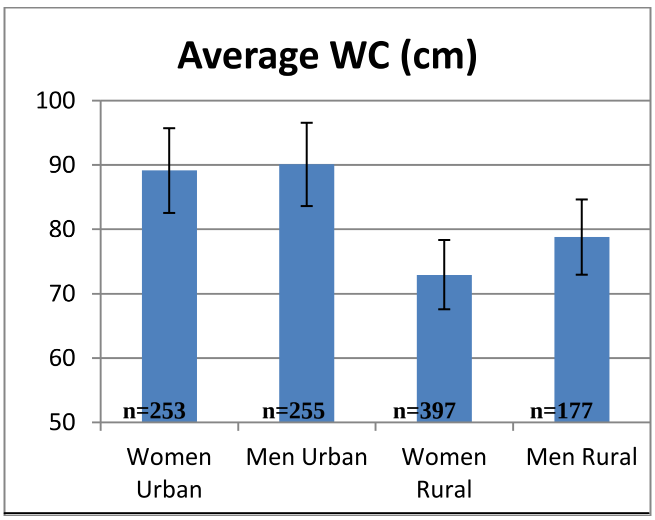
****Note:** Rupees (Rs) are the currency of India; 500 Rs is roughly equivalent to $10 US.*

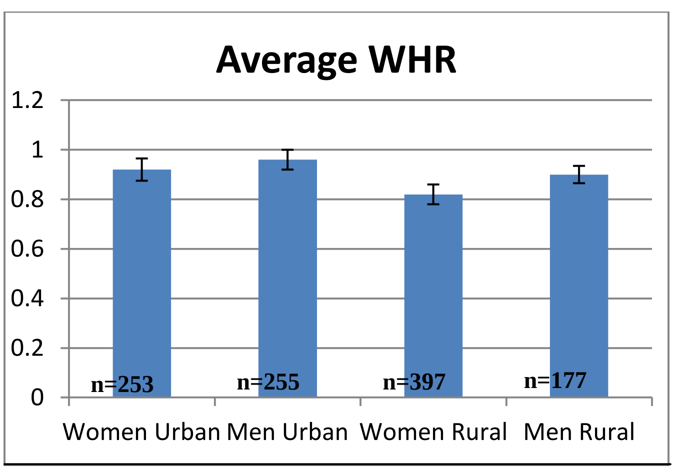
The data is stratified by gender (men or women) and location (rural or urban). The mean age of the men and women in the urban population is 43 ± 12.8 years and 42 ± 10.7 years, respectively. The overall mean age of the rural population was slightly less than the urban population with 41 ± 15.4 years for men and 39 ± 13.6 years for women. The men tend to have slightly lower BMI than women in both the rural and urban populations. The rural populations had lower BMI values than the urban population. WC was slightly higher among urban and rural men as compared to women. WC among urban men and women is much higher than rural men and women. WHR was highest among urban men (0.96), followed by urban women (0.92), then rural men (0.90) and then rural women (0.82). Among the four subpopulations, urban women had the highest prevalence of diabetes (13.8%) followed by urban men (13.3%), rural men (10.2%) and rural women (7.6%). Rural women had the least prevalence of T2DM and IFG. The urban men and women had a higher percentage of post high school education when compared to the rural populations. Urban women had the highest percentage of illiteracy and no formal education (30.8%) across all populations. Tobacco use was more common among men than women in both rural and urban areas. The rural population has a higher percentage of tobacco users when compared to the urban population. The average monthly income varies greatly between the urban and rural populations. Over half the rural populations (both men and women) make less than Rs 1500 or $33 US dollars per month. In contrast to this, over half the urban population makes approximately Rs 10,000 per month or $204 US dollars.

Graphs 5.1, 5.2 and 5.3 compare the mean BMI, WC, and WHR values across the urban and rural populations. The rural men and women have much lower BMI and WC values then the urban men and women. WHR are higher among both rural and urban men when compared to women.

Graph 5.1, 5.2, and 5.3: Comparison of Average Body Mass Index (kg/m^2), Waist Circumference (cm), and Waist-to-Hip Ratio for Urban and Rural Men and Women

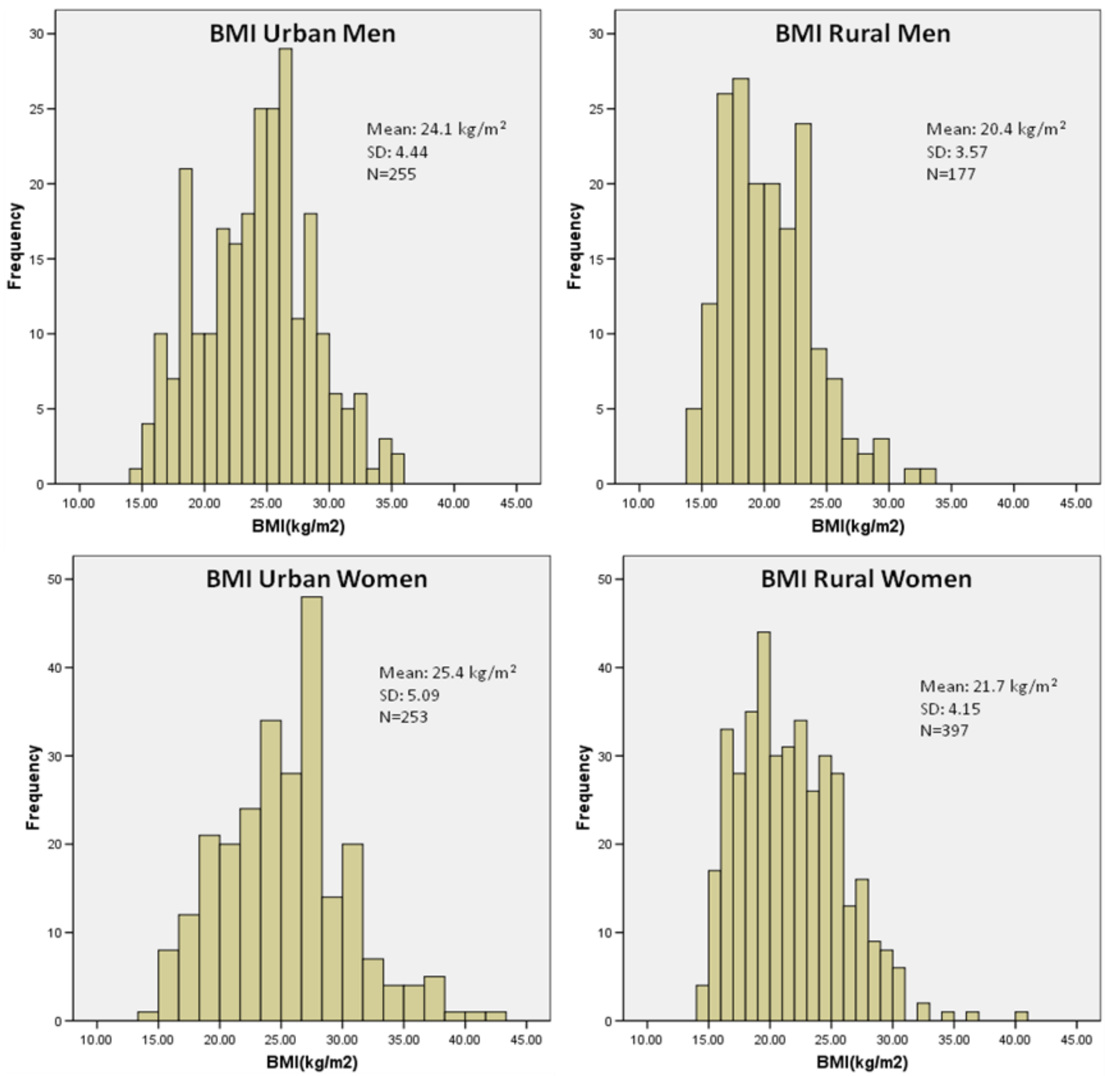




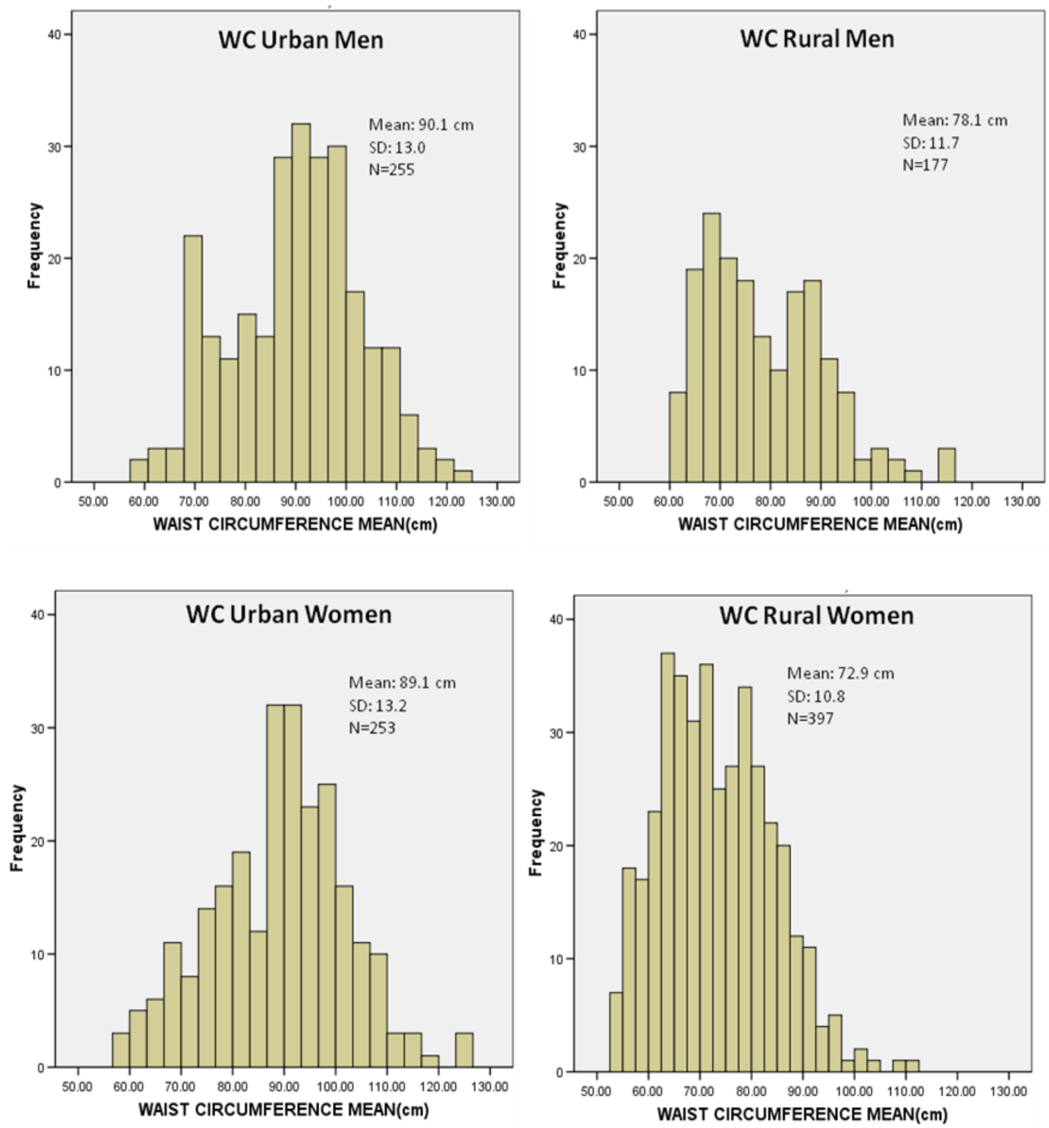


Graphs 5.4 through 5.10 show the distribution of BMI and WC values across the urban and rural populations. In all cases the data was normally distributed except BMI for urban women. This data was log-transformed and plotted. For the rural population, BMI, WC and WHR except for WHR in rural men were all logged. Even with the log of the parameters, the WHR for rural women was still positively skewed. Graphs 5.16-5.22 show the general distribution of the logged values for BMI, WC, and WHR for the non-normal distributions.

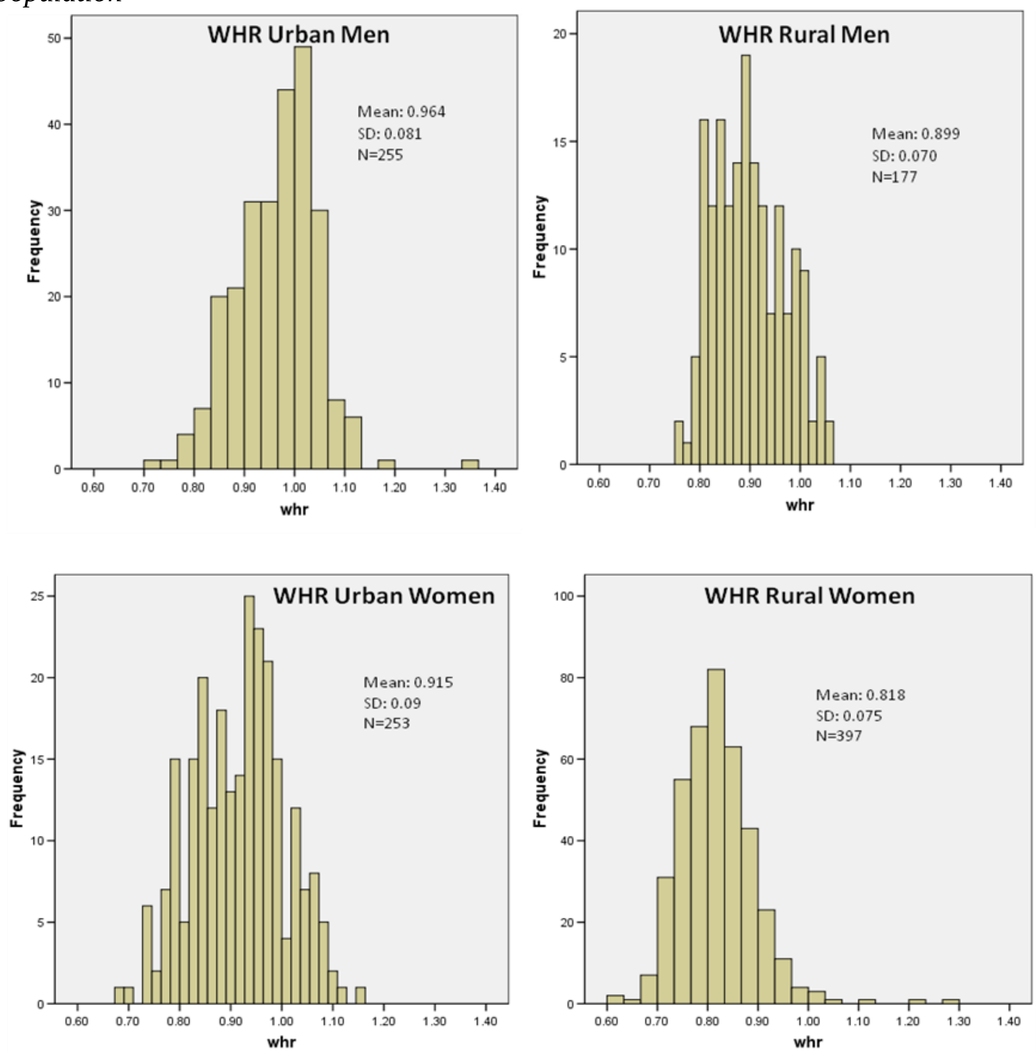
Graph 5.4- 5.7: General distribution of Body Mass Index (kg/m^2) values among urban and rural sample



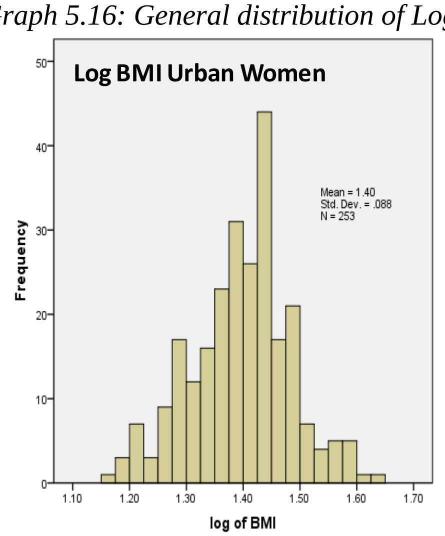
Graph 5.8-5.11: General distribution of Waist Circumference (cm) values of urban and rural sample population



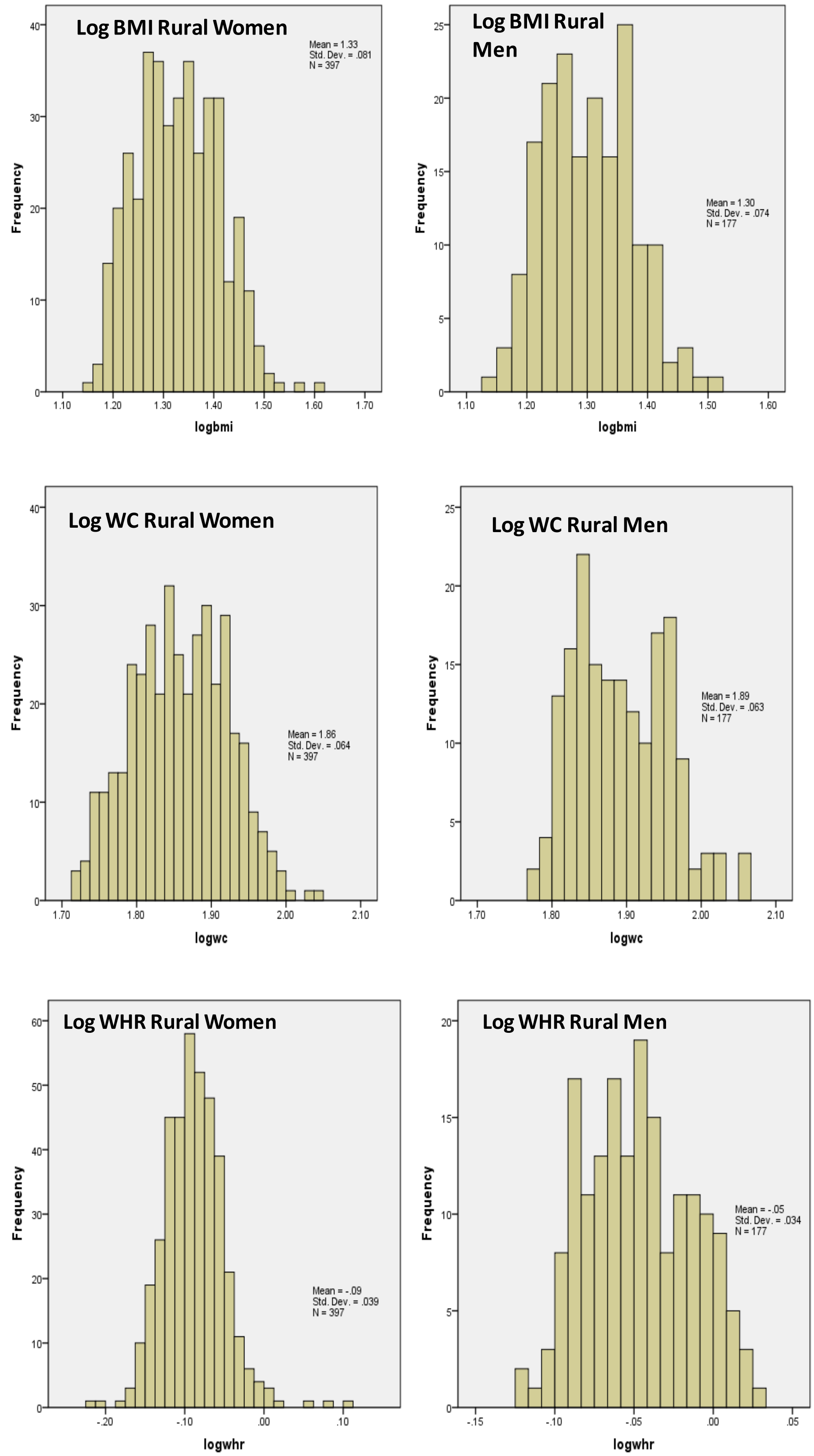
Graph 5.12-5.15: General distribution of Wais- to- Hip Ratio values of urban and rural sample population



Graph 5.16: General distribution of Log Body Mass Index (kg/m^2) values of urban women



Graph 5.17-5:22: General distribution of Log Body mass Index (kg/m2), Waist Circumference (cm) and Wais- t0- Hip Ratio values of rural men and women



Section 5.1: Prevalence of Diabetes at specified anthropometric cut points

Tables 5.2 -5.10 show the crude prevalence of subjects with diabetes, IFG and impaired glucose levels (diabetes + IFG) at specific BMI, WC, and WHR cutpoints.

Table 5.2: Prevalence of subjects with Type II Diabetes at specific Waist Circumference (cm) ranges

	Urban Men	**Urban Women**	**Rural Men**	**Rural Women**
	N (%) T2DM	**N (%) T2DM**	**N (%) T2DM**	**N (%) T2DM**
Overall	34 (100)	35 (100)	18 (100)	30 (100)
≤ 95 cm	17 (50)	13 (37.1)	17 (94.4)	26 (86.7)
≤ 90 cm	12 (35.3)	5 (14.3)	13 (72.2)	22 (73.3)
≤ 85 cm	2 (5.9)	2 (5.7)	4 (22.2)	18 (60)
≤ 80 cm	0 (0)	2 (5.7)	4 (22.2)	16 (53.3)
≤ 75 cm	0 (0)	2 (5.7)	3 (16.7)	8 (26.7)

Table 5.3: Prevalence of subjects with Type II Diabetes at specific Body Mass Index (kg/m^2) ranges

	Urban Men	**Urban Women**	**Rural Men**	**Rural Women**
	N (%) T2DM	**N (%) T2DM**	**N (%) T2DM**	**N (%) T2DM**
Overall	34 (100)	35 (100)	18 (100)	30 (100)
18.5-24.9	12 (35.3)	8 (22.9)	14 (77.8)	13 (43.3)
18.5-23.9	9 (26.5)	4 (11.4)	12 (66.7)	13 (43.3)
18.5-22.9	7 (20.6)	2 (5.7)	7 (38.9)	12 (40)
18.5-21.9	6 (17.6)	2 (5.7)	4 (22.2)	9 (30)
18.5-20.9	2 (5.9)	2 (5.7)	2 (11.1)	5 (16.7)

Table 5.4: Prevalence of subjects with Type II Diabetes at specific Waist-to-Hip Ratio ranges

	Urban Men	**Urban Women**	**Rural Men**	**Rural Women**
	N (%) T2DM	**N (%) T2DM**	**N (%)T2DM**	**N (%) T2DM**
Overall	34 (100)	35 (100)	18 (100)	30 (100)
≤ 0.90	0 (0)	5 (14.3)	4 (22.2)	18 (60)
≤ 0.87	0 (0)	2 (5.7)	1 (5.6)	17 (56.7)
≤ 0.85	0 (0)	2 (5.7)	0 (0)	12 (40)
≤ 0.82	0 (0)	2 (5.7)	0 (0)	5 (16.7)
≤ 0.80	0 (0)	1 (2.9)	0 (0)	2 (6.7)

Table 5.5: Prevalence of subjects with Impaired Fasting Glucose at specific Waist Circumference (cm) ranges

	Urban Men	Urban Women	Rural Men	Rural Women
	N (%) IFG	N (%) IFG	N (%) IFG	N (%) IFG
Overall	66 (100)	45 (100)	24 (100)	47 (100)
≤ 95 cm	42 (89.4)	30 (66.7)	22 (91.7)	46 (97.9)
≤ 90 cm	31 (47)	22 (48.9)	17 (70.8)	42 (89.4)
≤ 85 cm	21 (31.8)	14 (31.1)	8 (33.3)	39 (83)
≤ 80 cm	18 (27.3)	11 (24.4)	7 (29.2)	28 (59.6)
≤ 75 cm	10 (15.2)	6 (13.3)	3 (12)	20 (42.6)

Table 5.6: Prevalence of subjects with Impaired Fasting Glucose at specific Body Mass Index (kg/m^2) ranges

	Urban Men	Urban Women	Rural Men	Rural Women
	N (%) IFG	N (%) IFG	N (%) IFG	N (%) IFG
Overall	66 (100)	45 (100)	24 (100)	47 (100)
18.5-24.9	29 (43.9)	16 (35.6)	14 (58.3)	26 (55.3)
18.5-23.9	23 (34.8)	15 (33.3)	11 (45.8)	17 (36.2)
18.5-22.9	19 (28.8)	14 (31.1)	6 (25)	16 (34)
18.5-21.9	16 (24.2)	11 (24.4)	2 (8.3)	14 (29.8)
18.8-20.9	12 (18.2)	5 (11.1)	2 (8.3)	7 (14.9)

Table 5.7: Prevalence of subjects with Impaired Fasting Glucose at specific Waist-to-Hip Ratio ranges

	Urban Men	Urban Women	Rural Men	Rural Women
	N (%) IFG	N (%) IFG	N (%) IFG	N (%) IFG
Overall	66 (100)	45 (100)	24 (100)	47 (100)
≤ 0.90	15 (22.7)	16 (35.6)	8 (33.3)	43 (91.5)
≤ 0.87	11 (16.7)	11 (24.3)	5 (20.8)	36 (76.6)
≤ 0.85	5 (7.6)	10 (22.2)	3 (12.5)	32 (68.1)
≤ 0.82	0 (0)	6 (13.3)	0 (0)	21 (44.7)
≤ 0.80	0 (0)	6 (13.3)	0 (0)	13 (27.7)

Table 5.8: Prevalence of subjects with Impaired Fasting Glucose or Type II Diabetes at specific Waist Circumference (cm) ranges

	Urban Men	Urban Women	Rural Men	Rural Women
	N (%) IFG & T2DM	N (%) IFG & T2DM	N (%) IFG & T2DM	N (%) IFG & T2DM
Overall	100 (100)	80 (100)	42 (100)	84 (100)
≤ 95 cm	59 (59)	43 (53.8)	39 (92.9)	72 (85.7)
≤ 90 cm	43 (43)	27 (33.8)	30 (71.4)	64 (76.2)
≤ 85 cm	23 (23)	16 (20)	12 (28.6)	57 (67.9)
≤ 80 cm	18 (18)	13 (16.3)	11 (26.2)	44 (52.4)
≤ 75 cm	10 (10)	8 (10)	6 (14.3)	28 (33.3)

Table 5.9: Prevalence of subjects with Impaired Fasting Glucose or Type II Diabetes at specific Body Mass Index (kg/m^2) ranges

	Urban Men	Urban Women	Rural Men	Rural Women
	N (%) IFG & T2DM	N (%) IFG & T2DM	N (%) IFG & T2DM	N (%) IFG & T2DM
No Restriction	100 (100)	80 (100)	42 (100)	84 (100)
18.5-24.9	31 (31)	24 (30)	28 (66.7)	39 (46.4)
18.5-23.9	32 (32)	19 (23.8)	23 (54.8)	30 (35.7)
18.5-22.9	26 (26)	16 (20)	7 (16.7)	28 (33.3)
18.5-21.9	22 (22)	13 (16.3)	4 (9.5)	23 (27.4)
18.8-20.9	14 (14)	7 (8.8)	4 (9.5)	12 (14.3)

Table 5.10: Prevalence of subjects with Impaired Fasting Glucose or Type II Diabetes at specific Waist-to-Hip Ratio ranges

	Urban Men	Urban Women	Rural Men	Rural Women
	N (%) T2DM & IFG	N (%) T2DM & IFG	N (%) T2DM & IFG	N (%) T2DM & IFG
Overall	100 (100)	80 (100)	42 (100)	77 (100)
≤ 0.90	15 (15)	21 (26.3)	12 (28.6)	61 (79.2)
≤ 0.87	11 (11)	13 (16.3)	6 (14.3)	53 (68.8)
≤ 0.85	5 (5)	12 (15)	3 (7.1)	44 (57.1)
≤ 0.82	0 (0)	8 (10)	0 (0)	26 (33.8)
≤ 0.80	0 (0)	7 (8.75)	0 (0)	15 (19.5)

Urban women have the fewest diabetes cases at smaller measures in WC and BMI within the subpopulations. Examining a lower WC cutpoint for women at 90 cm excluded 85.6% of the T2DM patients. In the rural population, at WC cutpoint of 75 cm, 26.7% of the population has T2DM; lower BMI cutoff values has a less significant impact on reducing number of T2DM cases in this sample populations. At BMI cutpoint 18.5-21.9, 17.6% of urban men and 22.2% of rural women still have T2DM. The prevalence of IFG is still high even at lower BMI and WC levels. At BMI cutpoint of < 22 kg/m^2, 24% of the urban men and women and 29% of the rural women are still diagnosed with IFG. For WHR, the urban population had fewer cases of T2DM at WHR of 0.90. At this cutpoint there are no cases T2DM among urban men, while among urban women there is a nearly 86 percent reduction of T2DM cases when compared to a higher cutpoint. Fewer cases of T2DM for rural women appear at cutpoints of 0.82.

Section 5.2: Bivariate correlation

Bivariate correlation between covariates, T2DM and, T2DM combined with IFG and is shown in table 5.11.

Table 5.11 Bivariate Correlation between Type II Diabetes and combined Type II Diabetes and Impaired Fasting Glucose and metabolic risk variables

Bivariate Correlation of Study Population

		AGE	Education	Smoking	Income	T2D Family history	Systolic	Diastolic BP	BMI	WC	HC	WHR	
T2D	Pearson Correlation	0.243	-0.042	-0.006	0.095	0.084	0.302	0.193	0.150	0.208	0.076	0.282	Urban Males N=255
	Significance	0.000	0.505	0.927	0.132	0.181	0.000	0.002	0.017	0.001	0.229	0.000	
T2D & IFG	Pearson Correlation	0.192	-0.003	0.022	-0.013	-0.071	0.107	0.039	0.109	0.161	0.049	0.238	
	Significance	0.002	0.958	0.725	0.83	0.259	0.087	0.538	0.081	0.010	0.440	0.000	
T2D	Pearson Correlation	0.253	-0.157	0.05	0.026	0.000	0.244	0.130	0.203	0.257	0.042	0.352	Urban females N=253
	Significance	0.000	0.012	0.431	0.68	0.998	0.000	0.039	0.001	0.000	0.506	0.000	
T2D & IFG	Pearson Correlation	0.178	-0.003	0.024	-0.013	-0.071	0.206	0.139	0.225	0.262	0.063	0.331	
	Significance	0.005	0.958	0.704	0.83	0.259	0.001	0.027	0.000	0.000	0.316	0.000	
T2D	Pearson Correlation	0.276	-0.116	0.16	0.071	0.231	0.170	0.187	0.116	0.221	0.077	0.335	Rural Males N=176
	Significance	0.000	0.123	0.033	0.345	0.002	0.024	0.013	0.126	0.003	0.312	0.000	
T2D & IFG	Pearson Correlation	0.187	-0.138	0.118	-0.015	0.180	0.198	0.318	0.301	0.358	0.246	0.402	
	Significance	0.013	-0.067	0.117	0.839	0.160	0.008	0.000	0.000	0.000	0.001	0.000	
T2D	Pearson Correlation	0.215	-0.076	0.155	-0.027	0.187	0.175	0.124	0.176	0.246	0.114	0.268	Rural females N=393
	Significance	0.000	0.133	0.002	0.595	0.000	0.001	0.014	0.000	0.000	0.024	0.000	
T2D & IFG	Pearson Correlation	0.220	-0.072	0.163	-0.017	0.247	0.229	0.184	0.231	0.281	0.203	0.224	
	Significance	0.000	0.151	0.001	0.735	0.000	0.000	0.000	0.000	0.000	0.000	0.000	

The Pearson Correlation value (r) for T2DM and the covariates range from 0.039 to 0.352. The Pearson values for T2DM and IFG and their covariants range from 0.039 to 0.402. Covariants are considered statistically significant at 0.01. WHR showed the strongest correlation to prevalence of diabetes. WC showed the second strongest correlation followed by BMI. In general, age was shown to be significantly correlated to T2DM and IFG (r= 0.178 to 2.76). Education, hip circumference and income are not considered significantly correlated with T2DM and T2DM and IFG. Smoking is only considered statistically significant among rural women (r= 0.155, p= 0.002). Diastolic blood pressure was significantly correlated to diabetes in all cases except urban women; conversely systolic blood pressure was significantly correlated in all cases except rural men. Statistical significant was seen more frequently between the covariates and T2DM as compared to impaired glucose levels.

<u>*Section 5.3: Receiver Operating Curve (ROC)*</u>

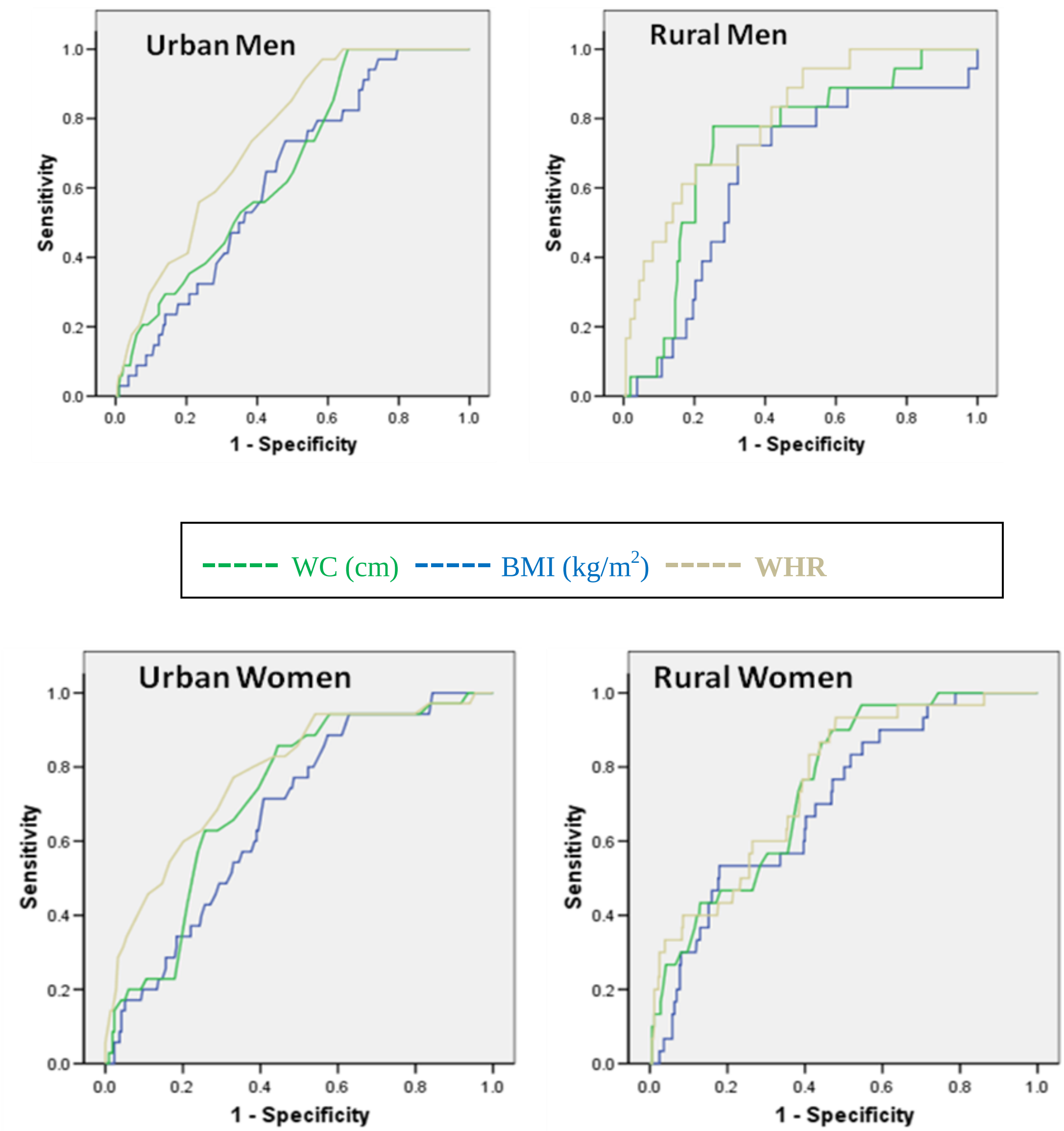
Table 5.12 summarizes the area under the ROC curve for the BMI, WC, and WHR. In all cases WHR has the largest area under the curve followed by WC and BMI, showing WHR to be the most strongly associated with T2DM.

Table 5.12: Area under the Receiver Operating Curve

	Area under ROC Curve		
	BMI	**WC**	**WHR**
Men Urban	0.629	0.658	0.748
Women Urban	0.673	0.722	0.782
Men Rural	0.645	0.730	0.799
Women Rural	0.704	0.750	0.757

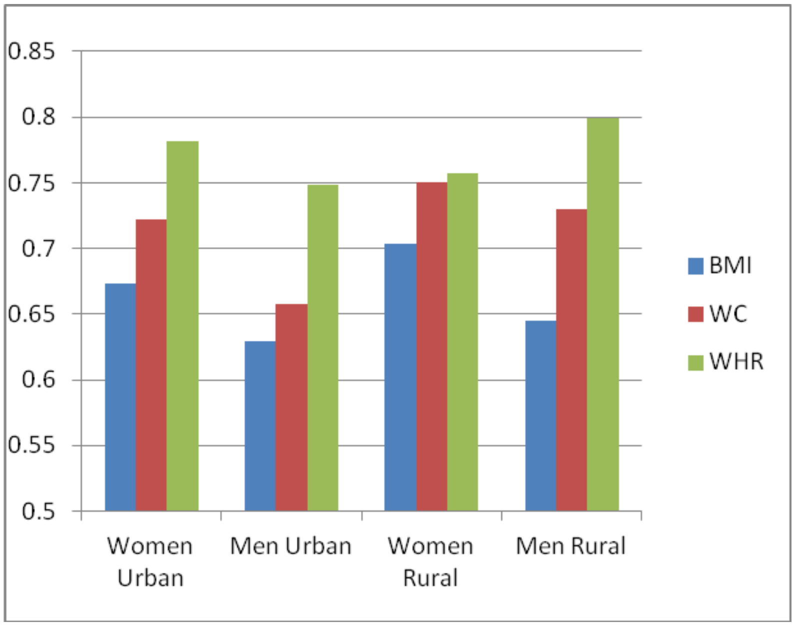
Graph 5.23 shows the ROC curves for all the urban and rural populations. Larger areas are observed in the rural populations for BMI, WC, and WHR as compared to urban populations. As demonstrated by a larger area under the ROC curve, WHR in both rural and urban populations is more strongly associated with T2DM than WC and BMI.

Graph 5.23: Waist Circumference (cm), Body Mass Index (kg/m^2) and Waist-to-Hip Ratio Receiver Operating Curves for Sample Populations



Graph 5.24 compares the areas under the curve across all populations for BMI, WC and WHR. The rural men have the highest area under the curve with WHR of 0.8.

Graph 5.24: Comparison of Area under the Receiver Operating Curve by gender and location



The recommended cutpoints based on the optimal area under the curve and the sensitivity and 1-specificity or false positive values are listed in Table 5.13. The suggested WC cutpoint of 86 cm and 85 cm was found for urban and rural men respectively, BMI of 24 kg/m^2 and 21 kg/m^2 and WHR of 0.90 and 0.86 respectively. The suggested WC for urban and rural women was 86 cm and 75 cm respectively, BMI of 25 kg/m^2 and 22 kg/m^2 and WHR of 0.84 and 0.93 respectively.

Table 5.13: Cutpoints for Body Mass Index (kg/m2), Waist Circumference (cm), and Waist-to-Hip Ratio

	WC			BMI			WHR		
	Cut Point	Sens.	1-Spec.	Cut Point	Sens.	1-Spec.	Cut Point	Sens.	1-Spec.
Urban Men	86	0.94	0.68	24	0.74	0.48	0.90	1.00	0.73
Urban Women	86	0.94	0.59	25	0.74	0.48	0.87	0.84	0.65
Rural Men	85	0.78	0.28	21	0.72	0.32	0.86	0.94	0.66
Rural Women	75	0.73	0.38	22	0.70	0.43	0.81	0.93	0.50

The odds ratio (OR) with a 95% confidence interval (CI) for the recommended BMI, WC and WHR cutpoints by rural and urban males and females are shown in table 5.14. Logistic regression model included all the variables that had significant bivariate correlation. These factors include BMI, WC, WHR, blood pressure, family history, and age. Smoking, income and education were controlled for but were not shown to be significantly associated to T2DM.

Table 5.14: Odds Ratio for sample population

	BMI (kg/m^2)		WC (cm)		WHR	
	Cutpoint	OR *(95% CI)*	Cutpoint	OR *(95% CI)*	Cutpoint	OR *(95% CI)*
Urban Men N=255	24	1.710 *(0.830, 3.524)*	86	2.61 *(0.989, 6.901)*	0.90	0*
Urban Women N=253	25	2.063 *(0.620, 6.871)*	86	0.901 *(0.687, 1.183)*	0.87	6.58 *(1.54, 28.01)*
Rural Men N=177	21	0.790 *(0.447, 1.395)*	85	0.910 *(0.760, 1.090)*	0.86	6.56 *(0.857, 50.297)*
Rural Women N=397	22	0.938 *(0.735, 1.198)*	75	0.979 *(0.911, 1.052)*	0.81	7.77 (1.836, 32.840)

**Note: OR: Odds Ratio, CI: Confidence Interval*
Covariates: Age, blood pressure, education, smoking, T2DM family history, income

For both men and women in the urban and rural sample populations, the OR is highest with WHR, followed by WC and BMI. Urban women are the only group that does not have the OR for WC greater than BMI. For urban men, at the recommended cutpoint for WHR of 0.90, there were zero reported cases of T2DM therefore the odds ratio could not be calculated for this cutpoint.

Chapter 6: Discussion

The present study found that WHR ratio had a stronger association with T2DM than WC and BMI. This is not in agreement with the WHO report stating that WC is the best way to measure abdominal obesity (WHO Expert Consultation, 2002). There are other studies that have looked at the association between anthropometric measurements and T2DM and found that there is no significant evidence that any single anthropometric measure of obesity (BMI, WC, and WHR) is a better predictor of metabolic risk and T2DM (Taylor, 2010; Qiao, 2009).

Conversely, there are studies that agree with the results of the present findings, and show that WHR is the variable most strongly associated with T2DM as compared to WC and BMI. In 2008, Kaur et al assessed the association of four obesity-related indices; BMI, WC, WHR, and waist-to-stature ratio (WSR), with hypertension and T2DM among 2148 men in two industrial units in Chennai, India. The study found that only WHR showed significant association with T2DM using logistic regression while BMI and WC showed significant association with hypertension. These results also concur with results from Arab population in the Middle East to determine optimal cutpoints for BMI, WC and WHR as a predictor for coronary heart disease (Al-Lawati, 2008), one of the co-morbidities of obesity as defined by the WHO in Table 1.1. That study found that WHR, as demonstrated by a larger area under the ROC curve, was strongly associated with coronary heart disease followed by WC and BMI. Based on the results from the present study, and the conclusions drawn by Kaur 2008 and Al-Lawati 2009 studies, the use of WHR as a screening method to identify risk for T2DM should be considered.

The cutpoints identified by the ROC curve for BMI, WC, and WHR are much higher for urban men and women than rural men and women. The urban cutpoints are closer to the recommended numbers for non-Asian populations by the WHO (WHO, 1997). Alternatively, the rural population has cutpoints that are the same or lower than the WHO Asian Specific standards. The identified cutpoints for the rural populations agree more closely with a study of the urban population that took place in Chennai, India The suggested cutoff values from this study are BMI of 23 kg/m^2 for both men and women, WC 85 and 80 for men and women respectively and WHR of 0.88 and 0.81 respectively (Snehalatha, 2003). The WC cutpoint suggested for both rural and urban men by the ROC curve is 85 and 86 cm respectively. These values are below the WHO Asian specific guideline of 90 cm. The recommended WC cutpoint of 86 cm for urban women is higher than the WHO Asian specific guidelines of 80 cm. Conversely, rural women have a much lower WC (75 cm) then suggested by the WHO.

<u>Section 6.1: T2DM prevalence at specified BMI and WC Cutpoints</u>

In the present study, urban men and women had a higher prevalence of T2DM and IFG than rural populations, which agrees with earlier studies (Boddula, 2008). At WC $\leq$85 cm, there were 95% fewer urban men and women with T2DM than at higher WC cutpoints. These results were not consistent with the predicted values by the WHO, which suggest Asian specific cutpoints at WC $\leq$80 cm for women and WC

≤ 90 cm for men. In our study a WC cutpoint of 90 cm for men according to the WHO recommended cutpoint identified 30% more cases of diabetes in urban men and 50% in rural men. Over half (53%) of the prevalent cases of T2DM among the rural women were seen at the current recommended WHO WC cutpoint for Asian women (80 cm). By lowering the WC cutpoint to 75 cm 73.4% fewer cases of T2DM among rural women were observed. Lowering the WC cutpoint for men to 85 cm agrees with a study by Lear et al (2009) which suggested cutpoints of 85cm and 80 cm for Asian men and women respectively.

The WHR cutpoints suggested by Lear et al (2009) are 0.90 and 0.80 for men and women respectively. In the present study, rural women and urban men had cutpoints that agree with these suggestions. Rural men had a suggested cutpoint for WHR closer to 0.85, while urban women had a suggested cutpoint much higher than 0.80 (0.87). Among urban men sampled, there were no cases of T2DM below the WHR cutpoint of 0.9. For rural men, a WHR cutpoint of 0.87 showed 94% fewer prevalent cases of T2DM.

Similar trends are seen for BMI. By examining a BMI cutpoint of < 25 kg/m^2 there was 87% fewer urban women and 65% fewer urban men with cases of T2DM. In the rural population a larger number of men and women had T2D at lower cutpoints than the urban population. Specifically, 22% rural men and 30% rural women had T2DM at BMI cutpoint of < 22 kg/m^2.

It is of interest to note that 35% of urban men and 72% of rural men without abdominal obesity (WC< 90 cm) had diabetes. This shows that the risk of developing diabetes can start at BMI and WC ranges that have been identified as normal for the

Indian population ((Deepa, 2009). Additionally, the high percentage of T2DM identified among individuals with WC $\geq$ 90 cm suggests the need to consider a lower cutpoint for WC in Asian Indian men. There is a large variation among urban and rural women in T2DM incidence at different anthropometric cutpoints. Five percent 53.3% of rural women at the same cutpoint have T2DM. WHR follows similar trends, at WHR of 0.80, 13% and 27.7% of urban and rural women respectively had T2DM.

The large variation in diabetes prevalence between the urban and rural populations across different BMI, WC, and WHR ranges suggests the need for specific cutpoints for urban and rural populations. However, the populations surveyed were from different geographical regions and may have very different environmental risk factors such as diet, smoking habits, physical activity and genetic predisposition. India is an ethnically and culturally diverse, heterogeneous country, with a population of 1.1 billion, and a variety of cultures, dialects and customs (Ali, 2009). There is a need to look at the individual states and rural and urban areas within India to get a more accurate picture of the current diabetes disparity.

Previous studies by Snehalatha et al (2003) and Deepa et al (2009), suggest that WC had the greatest association with T2DM. Our research found that WHR was more strongly associated with T2DM then WC and BMI. These results are in agreement with data by Pua and Ong (2005) which showed that obesity indicators (BMI, WHR, WC) were complimentary to one another, but that WHR is the best discriminator for T2DM (Pua, 2005).

Section 6.2: ROC Curve Analysis

The area under the ROC curve showed that WHR has a larger area, and therefore is a better predictor of T2DM followed by WC, and BMI for all Indians. The cutpoints identified within the study are higher for the urban population than those seen in earlier studies, and lower for the rural populations. Both the Chennai Rural Urban Epidemiology Study (CURES) and National Urban Diabetes Study (NUDS) suggest a BMI cutpoint of 23 kg/m^2 (Deepa, 2009; Snehalatha, 2003). Our analysis suggests cutpoints of 25 kg/m^2 for urban women, 24 kg/m^2 for urban men and 22 kg/m^2 for rural women and 21 kg/m^2 for rural men. The large difference in suggested BMI cutpoints between the rural and urban populations was unexpected.

The suggested WC cutpoint for both rural and urban men is below the current Asian specific standards and is in agreement with other studies. In the NUDS study, the suggested WC for urban men is 85 cm and 80 cm for urban women (Snehalatha, 2003). Our analysis showed WC cutpoints for the urban and rural men were in agreement with the NUDS suggested WC cutpoint. Conversely the WC cutpoint (86 cm) for urban women is higher than that suggested by the NUDS study of 80 cm while that of rural women was much lower (WC of 75 cm). The current WHO Asian specific suggested cutpoint for men is higher than what our analysis shows at 90 cm. Conversely, the WHO Asian specific WC guidelines for women (80 cm) are lower than what is seen in our analysis for the urban population, and too high for the rural population.

The variation in results for BMI, WC, and WHR between urban and rural populations is unexpected. It was expected that the urban population would have

BMIs and WCs higher than the rural population, but that both subpopulations would have cutpoints within or lower than the WHO Asian-Specific suggested cutpoints shown in Table 1.3. The results show suggested cutpoints closer to the non-Asian specific WHO standards as shown in Table 1.2.

The WHO does not have an Asian specific suggested WHR cutpoints but a committee met in 2008 to discuss the use of WHR versus WC in assessing the correlations of these anthropometric indices with metabolic risk complications. The use of WHR to assess metabolic risk is a deviation from earlier reports, which stated that WC is accepted as a better method to correlate metabolic risk factors to abdominal obesity (WHO Expert Consultation, 2004). In the proceedings that were published in 2011, the WHO suggests the following guidelines for WHR; ≤ 0.90 and ≤ 0.85 in men and women respectively. In this report, the WHO does not state which of these two measurements of abdominal obesity is better. They further address the need for country specific guidelines for WHR. (WHO Expert Consultation, 2011). These suggested values agree with the suggested cutpoints shown in the urban men and women, but disagree with the Asian cutpoints suggested by Lear et al (2009) for women of WHR= 0.80, which more closely agrees with the suggest WHR cutpoint found for rural women.

The areas under the ROC curve are not as large as expected. An area of 0.6 is only 10% better than chance (50/50 odds) at predicting T2DM. The ROC curves for WC are marginally better than BMI, but still have areas only within the 70% range. The areas shown in the present study have numbers that agree with other studies that have looked at WC and BMI, and their associations with T2DM. In the CURES study, when controlling for the other covariates, the max area under the curve for BMI is 0.66 for both men and women, and WC is 0.70 and 0.69 for men and women respectively (Deepa, 2009). This data suggests that BMI or WC should not be used alone as a method to assess T2DM risk in individuals.

Section 6.3: Summary

India leads the world in diabetes cases. In the present study, we looked at a subset of an urban and rural Indian population and evaluated the association of anthropometric indices (BMI, WC and WHR) with T2DM. In both the rural and urban sample populations, women have a higher BMI and lower WC and WHR values than men in the same area. The BMI, WC, and WHR values are significantly higher among both men and women in the urban population as compared to the rural populations. This agrees with previous studies suggesting that rural populations in India have lower BMI, WC and T2DM values than urban populations. The overall prevalence of T2DM and IFG shown in the two subpopulations is higher than rates seen in European populations. This may be explained by Asian Indians having a greater susceptibility to T2DM and IFG as compared to Europeans (Snehalatha, 2003). Obesity rates, insulin resistance and T2DM prevalence has increased in India in the last ten years. The rates shown in the present study agree with those shown in similar studies for other Indian subpopulations (Subramanian, 2009, Misra, 2011 and Deepa, 2009).

The most notable findings in the present study found that the anthropometric indicators (BMI, WC and WHR) are significantly associated with T2DM, and WHR have the strongest association, followed by WC and then BMI. The recommended cutpoints determined from the ROC curve suggest cutpoints for the urban population that are larger than expected.

The hypothesis that rural populations will have lower prevalence of T2DM and IFG was confirmed. The ideal cutpoints for BMI, WC, and WHR determined by the ROC curve for each sample population had large variations between the urban and rural populations. As a result of the variation between urban and rural populations, a defined cutpoint for Asian Indians could not be determined. The large variation between the rural and urban samples, suggests the need for independent cutpoint for each state within India. It is impossible to generalize or extrapolate data from one part of India to another because of the genetic and ethnic variances as well as variation in dietary intake and other environmental factors seen within the country (Ali, 2009). Based on these results, BMI, WC, and WHR are shown to be useful tools in identify T2DM risk but no measure should not be used alone.

Section6.4: Limitations of the Study and Future Research

The survey questionnaire administered for the study was very detailed, with several pages of questions detailing physical activity and diet. Because of the complexity and variation of these questions, we did not include physical activity and diet into our analysis. As a result, physical activity and diet were not controlled within the sample populations.

There is possible variation across results for anthropometric measurements within the rural and urban populations because different individuals took these measurements. However, consistent training between all groups was given, so the variations in measurement between individual populations are expected to be negligible.

Future research should explore using WHR as compared to WC to assess T2DM risk in other Indian populations. Seventy percent of Indians live in rural India, yet most of the T2DM studies take place in urban India (Misra, 2011). Additional studies should focus on looking a T2DM rates and prevention methods in rural India.

A multi-state, cross country integrated study needs to be funded to get a better understanding of T2DM prevalence across India, so that accurate assessments can be made. Previous studies have shown that there is a widespread disparity of diabetes prevalence among the regions of India. The prevalence can range from 2.4-7.5% in North India to 2.1-13.2% in Southern India (Misra, 2011). This type of study would be difficult, because of the huge population of India.

Another limitation of the present study is differences in the number of participants between the rural and urban sample. This difference in population was a result of availability of the sample population. The number one cited reason for men not able to participate in the rural study was the inability to take time off of work. In addition to understanding the prevalence of T2DM in India, additional effective methods must be developed to educate the public on ways to prevent and manage T2DM. This research should focus on reaching the rural population since 70% of the Indian population lives in rural areas of the country. General education should focus on teaching people about T2DM prevention through diet and physical activity as well as treatment options. Additionally, education should focus on informing individuals about prediabetes or IFG risk to help increase screening and early detection and reduce the number of individuals diagnosed with T2DM. Along with prevention and education, simple methods for screening large populations should be developed. The present study showed that BMI, WC, and WHR are effective methods to screen for T2DM risk, but these should not be used alone as there were individuals that had normal BMI and WC but were still diabetic. A program that looks at affordable and easily accessible screening methods for large populations would contribute to the overall understanding of T2DM.

In a study published in 2010, the predicted direct and indirect costs associated with diabetes in India for 2010 was between $25.5 -38 billion dollars (Tharkar, 2010). The present study did not look at the cost of diabetes care and treatment options across urban and rural populations. Given the disparity between urban and rural monthly incomes seen in the present study, a future study that looks at the cost of diabetes treatment and treatment availability in urban and rural areas would be of interest. This study would highlight the possible economic burden to India that diabetes will have.

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