Metabolic Syndrome and Insulin Resistance in Pakistan:

a population based study in adults 25 years and above in Karachi

Muhammad Zafar Iqbal Hydrie

Thesis submitted as a part of the
Master of Philosophy Degree in International Community Health

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Abstract

Background : Sedentary lifestyle along with easy access to fast foods have resulted in a global epidemic of diabetes with a prediction that it will rise from the current estimate of 190 million to 324 million in 2025. WHO predicts that 170% increase of diabetes will be in the developing countries. Type 2 diabetes (T2DM) has become one of the major causes of premature illness and death and cardiovascular disease (CVD) will be responsible for up to 80% of these deaths. So it seems that at the moment we are faced with the twin pandemic of T2DM and CVD and the brunt of this would be borne by the developing countries. The clustering of central obesity, dyslipidaemia, hypertension, and hyperglycaemia known as metabolic syndrome has been associated with a 2-3 fold increase in T2DM and CVD. It is recognized that the features of the metabolic syndrome can be present 10 years preceding T2DM and CVD. The prevalence rates of metabolic syndrome appear varied using the WHO, EGIR, AACE, ATP III and IDF definitions. Therefore it is needed to study the suitability of metabolic syndrome definitions in this population.

Objective: To estimate the prevalence of metabolic syndrome in adults aged 25 years and above from an urban population of Karachi.

Methods: The survey was conducted from July to December 2004 by generating a computerized random sample of 500 households from houses in Lyari Town using a Geographical Imaging System (GIS). The survey activities were divided into two phases—the household interview and blood sample collection. Field work entailed visits to the selected household by a field team (medical students and health worker), introduction to the purpose of the research study, consent, interviews and physical measurements. In the 532 households visited 867 adults $\geq$ 25 years old consented to take part in the survey out of which 363 gave blood samples.

Results: Prevalence of Diabetes was 9.4% while 5.6% had impaired fasting glucose (Abnormal glucose tolerance 15%). Prevalence of metabolic syndrome was found to be 49% by modified ATP III, 34.8% by IDF, 16.9% by AACE, 15.2% by EGIR and 7.4% by WHO definition. Insulin resistance defined by 75th percentile of HOMA-IR was measured as 1.94.

Conclusion: Inclusion of modified waist circumference and BMI cutoffs may help to predict metabolic syndrome more precisely as incorporated in modified ATP III and IDF definition. The rising prevalence of obesity and metabolic syndrome has received increased attention in recent years as both place individuals at risk for T2DM and CVD. Thus epidemiological and intervention trial studies which support lifestyle changes as the main modifiable risk factor in the treatment of individual components of the metabolic syndrome can then be initiated.

Key Words: Prevalence, Metabolic Syndrome, IDF Definition, Diabetes, Pakistan, WHO, Modified ATP III

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List of Acronyms

ADA	American diabetes association
AACE	American Association of Clinical Endocrinology
BMI	Body mass index
CHOD-PAP	Cholesterol Oxidase – Para amino phenazone
CHD	Coronary Heart Disease
CVD	Cardiovascular Disease
EGIR	European Group for the Study of Insulin Resistance
GOD-PAP	Glucose Oxidase – Para amino phenazone
GPO-PAP	Glycerol Phosphate Oxidase –Para amino phenazone
HOMA	Homeostasis model assessment
IDF	International Diabetes Federation
LDL	Low density lipoprotein
MS	Metabolic Syndrome
NCEP – ATP III	National Cholesterol Education Program : Adult Treatment Panel
HDL	High density lipoprotein
TGs	Triglycerides
T2DM	Type 2 Diabetes Mellitus
WHO	World Health Organization

Chapter 1. Introduction

1.1 Background - Diabetes Mellitus and CVD

Changes in work patterns from heavy labour to sedentary, the increase in computerization and mechanization, and improved transport are just a few of the changes that have made an impact on human health (1). These sedentary changes along with easy access to fast foods and empty calories have resulted in escalating rates of both obesity and type 2 diabetes globally (2,3). Paradoxically, part of the problem relates to the achievements in public health during the 20th century, with people living longer owing to elimination of many of the communicable diseases (4). Non-communicable diseases (NCD) such as diabetes and cardiovascular disease (CVD) have now become the main public health challenge for the 21st century, as a result of their impact on personal and national health system and the premature morbidity and mortality associated with the NCDs (1,5).

1.1.1 Diabetes Mellitus

Diabetes mellitus is a metabolic disorder with both genetic and lifestyle etiologies that results in abnormal glucose control. It is a chronic disease caused by inherited and/or acquired deficiency in production of insulin by the pancreas, or by the ineffectiveness of the insulin produced. An acquired deficiency may be triggered by life style factors. However a deficiency of insulin results in increased concentrations of glucose in the blood, which in turn damages many of the body's systems. Genetics has an influential role on the epidemiology of the disease.

1.1.2 Global Burden of Diabetes

The global figure of people with diabetes is set to rise from the current estimate of 190 million to 324 million in 2025 (6,7). WHO predicts 170% increase in the number of people with diabetes for the developing countries (6).The greatest increase is projected in India (195%) (6).

The past two decades have seen an explosive increase in the number of people diagnosed with diabetes worldwide and 75% of these will be from the developing countries (6). This trend of increasing prevalence of diabetes and obesity has already imposed a huge burden on health-care systems and this will unfortunately continue to

increase in the future (1,8). The magnitude of the problem has caught the public health community by surprise.

Each year, 3.2 million people around the world die from complications associated with diabetes. In countries with a high diabetes incidence, such as those in the Pacific and the Middle East, as many as one in four deaths in adults aged between 35 and 64 years is due to the disease. Type 2 diabetes has become one of the major causes of premature illness and death, mainly through the increased risk of CVD which is responsible for up to 80 per cent of these deaths (7,9).

Type 2 diabetes (and its associated hyperglycaemia or dysglycaemia) is a manifestation of a much broader underlying disorder – the metabolic syndrome (3,10). This includes a cluster of CVD risk factors that, in addition to glucose intolerance (that is, IGT or diabetes), includes hyperinsulinaemia, dyslipidaemia, hypertension, visceral obesity, hypercoagulability and microalbuminuria.

1.1.3 Ischemic Heart Disease

Ischemic Heart Disease (IHD) - also known as Coronary Heart Disease (CHD) - refers to a group of closely related syndromes caused by an imbalance between myocardial oxygen demand and blood supply (11,12). The most common cause of IHD is a reduction in coronary arterial blood supply due to atherosclerosis of the coronary arteries (12).

1.1.4 Global Burden of Cardiovascular Disease

It is estimated that 17 million people died of cardiovascular diseases (CVD) during 2001(13). The most common reported types of CVD were IHD, hypertension (HTN) and rheumatic heart disease (13). The World Health Report 1999 estimates that 31% of all deaths in 1998 as well as 10% of the total disease related burden in terms of Disability Adjusted Life Years loss (DALYs) were attributable to CVD (14).

The metabolic syndrome has been associated with a 2–3 fold risk of cardiovascular disease and more important than this is the clustering of the heart attack risk factors in this syndrome: diabetes and raised fasting plasma glucose, abdominal obesity, high cholesterol and high blood pressure (15-17).

Developed Countries

The rates of CVD are comparable or higher among persons of African origin than those found in whites in the US (18). In Western Europe, CVD is responsible for about one third of all deaths (12,18). Eastern European countries such as the Ukraine, the Russian Federation, Hungary, and the Czech Republic have among the highest CVD rates in the world which is still rising. This is in marked contrast to the more economically stable Western European countries where declines in CVD mortality rates have been observed over the past 30 years (19).

Developing Countries

Globally low and middle income countries account for 78% of all CVD-attributable deaths and 86% of all CVD-attributable DALY loss (14). As far back as 1990, developing countries accounted for 63% of all CVD deaths and 74% of CVD related DALY loss (20). It has been estimated that 5.3 million deaths attributable to CVD occurred in developed countries in 1990, whereas the corresponding figure for developing countries ranged between 8 to 9 million [i.e., a relative excess of 70%] (21).This CVD burden afflicts both men and women, with CVD accounting for 34% of all deaths in women and 28% in men during 1998 (14). The high burden of CVD in developing countries is attributable both to the increased incidence of these disorders as well as the relatively early age at which they manifest (13,22-26). For example, 47% of the deaths attributable to CVD in developing countries in 1990 occurred below the age of 70 years, in contrast to 23% of such deaths in high income industrial countries (27). The contribution of developing countries to the global burden of CVD in terms of disability adjusted years of life lost was three times higher than that of developed countries (28).

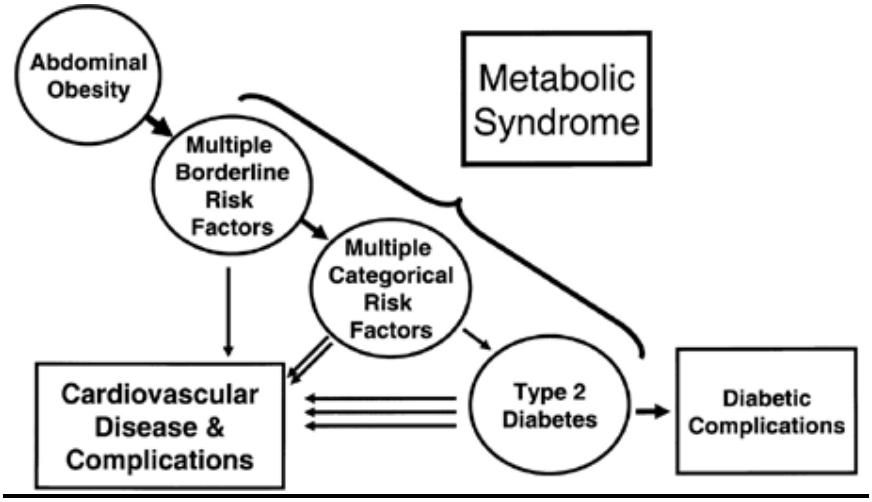


Figure 1: Metabolic Syndrome - Clustering of CVD Risk Factors

1.2 Metabolic Syndrome (Diabetes and CVD Epidemic)

Over the last 20 years, the prevalence of the metabolic syndrome has steadily increased in all populations worldwide making this one of the major global public-health challenges (15). The ultimate importance of the metabolic syndrome is that it helps to identify individuals at high risk of developing both type 2 diabetes and cardiovascular disease (CVD).

It is estimated that around 20-25 per cent of the world's adult population have the metabolic syndrome and they are twice as likely to die from and three times as likely to have a heart attack or stroke compared with people without the syndrome (29).

In addition, people with metabolic syndrome have a fivefold greater risk of developing type 2 diabetes (30). They would add to the 230 million people worldwide who already have diabetes, one of the most common chronic diseases worldwide and the fourth or fifth leading cause of death in the developed world (31). The clustering of cardiovascular disease (CVD) risk factors that typifies the metabolic syndrome is now considered to be the driving force for a new CVD epidemic.

This 'clustering' of metabolic abnormalities that occur in an individual appear to confer a substantial additional cardiovascular risk over and above the sum of the risk associated with each abnormality (32,33). Thus it appears that the more components of the metabolic syndrome that are evident, the higher is the cardiovascular mortality rate (34). And at the moment we are faced with the twin pandemics of T2DM and

cardiovascular disease and that the brunt of this would be borne by many poor and developing countries (6, 28).

1.2.1 History of the Metabolic Syndrome

One of the earliest descriptions of the metabolic syndrome was by Kylin in 1923 when he described the involvement of hypertension, hyperglycemia, and high uric acid levels (35). In the late 1940s and early 1950s, Jean Vague presented a series of reports on the sexual differentiation of obesity and its consequences. Vague later identified the masculine form of abdominal obesity and described the relationship between abdominal obesity, fat distribution and their association with diabetes and other chronic disorders (36,37). In 1987 he presented a updated review of what he termed as “diabetogenic obesity” in a lecture at the Fifth International Congress on Obesity (38). In the early 1960s, Avogaro and Crepaldi described a syndrome, which involved hypertension, hyperglycemia, and obesity (39). Camus was another early observer of these associations and in 1966 he identified the “trisyndrome métabolique” to include goutte, diabéte, and hyperlipémie (40). Later in the late 1970s Pyorala also showed strong links between glucose intolerance, hyperinsulinemia, and coronary heart disease in a study of two sets of the Finnish population (41). In the 1980s, Modan et al. also described this link between obesity, hypertension, and cardiovascular disease (CVD) (42).

In 1988 Reaven described “a cluster of risk factors predisposing a person towards diabetes and cardiovascular disease” naming this as Syndrome X. This was the first time that the insulin resistant state was implicated as being central to this collection of cluster of risk factors of Syndrome X (43).

After Reaven put forward his concept of Syndrome X, there were many attempts to introduce the concept of risk factor clustering for cardiovascular disease and type 2 diabetes mellitus (T2DM) into the general clinical arena with different names such as “deadly quartet” and “insulin resistance syndrome” etc but for some time now this has come to be referred as the “Metabolic Syndrome”.

1.2.2 Evolution of Metabolic Syndrome Definition - towards a global consensus

In 1998 the World Health Organization (WHO) published the definition of metabolic syndrome closely followed in the next year by European Group for the Study of Insulin Resistance (EGIR) (44,45). In 2001 the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) came out with their definition, followed in 2003 by the American Association of Clinical Endocrinologists (AACE) (46,47), and most recently that of the International Diabetes Federation defined in 2005 (48). In 2005, National Heart, Lung, and Blood Institute; American Heart Association came up with the criteria which slightly modified the ATP III definition (49).

Thus the first attempt to define this syndrome was in 1998 by a WHO diabetes group which had insulin resistance, impaired glucose tolerance or diabetes, as essential components, together with at least two other components (Table 1).

In 1999, the European Group for Study of Insulin Resistance (EGIR) reverted to the term insulin resistance syndrome (45). Insulin resistance; a primary requirement was defined as plasma insulin levels in the upper quartile of the population. Predetermined cut points for the other criteria were used (Table 1). EGIR focused more on abdominal obesity than did WHO, but in contrast to WHO, EGIR excluded patients with type 2 diabetes mellitus from their definition.

In 2001, the National Cholesterol Education Program, Adult Treatment Panel III (NCEP, ATP III) introduced an alternative clinical criteria for defining the metabolic syndrome, with the aim of identifying people at long-term risk for ischemic heart disease (46). While insulin resistance was recognized as been important, the requirement was excluded from the definition. The ATP III criteria did not mandate the requirement of any single factor for diagnosis, but instead made the presence of three of five factors as the basis for establishing the diagnosis; these factors being abdominal obesity, elevated triglycerides, reduced HDL-C, elevated blood pressure, and elevated fasting glucose (IFG or type 2 diabetes mellitus) (Table 1).

In 2003, the American Association of Clinical Endocrinologists brought the focus back on insulin resistance as the primary aetiology underlying the primary metabolic risk factors (47). Calling it the insulin resistance syndrome, the definition included major criteria, which were IGT, elevated triglycerides, reduced HDL-C, elevated blood

pressure, and obesity. Other factors needed to form clinical judgment were a family history of CVD or type 2 diabetes mellitus, polycystic ovary syndrome, and hyperuricemia. They did not specify any absolute requirement or even the number of factors, which had to be present to merit the diagnosis of the metabolic syndrome rather leaving the diagnosis to the clinician's judgment (Table 1).

In 2005, the International Diabetes Foundation (IDF) published their criteria and tried to keep the requirements for the diagnosis of the metabolic syndrome as clinically simple and widely usable as possible (48). The IDF clinical definition made the presence of abdominal obesity obligatory for diagnosis. Once this essential condition was present, at least two additional factors out of four were necessary for the diagnosis. The IDF definition recognized and emphasized ethnic differences in the correlation between abdominal obesity and other metabolic syndrome risk factors. The criteria of abdominal obesity were specified by nationality or ethnicity based on best available population estimates. (Table 1).

Also in 2005, the AHA/NHLBI statement, kept to the basic ATP III criteria except for few minor changes (46,49). The AHA/NHLBI diagnostic criteria for metabolic syndrome [49], popularly known as the modified ATP III definition, has no mandatory criteria which had to be present. One major change was the reduction from 110 to 100 mg/dl for the diagnosis of IFG; this adjustment corresponded to the recently modified American Diabetes Association (ADA) criteria for IFG (Table 1).

Different ethnic backgrounds, diets, levels of physical activity, population age and sex structure and levels of nutrition, all influence the prevalence of the metabolic syndrome making it even more difficult to identify a predictive definition. What we know is that this syndrome predicts high risk of cardiovascular disease and diabetes (50).

Unfortunately the concept and definition of the metabolic syndrome are still subject to debate (51,52), including the applicability of a single definition to people of different ethnic origin (15). Whether any current definition of the metabolic syndrome is a better predictor than the others as a marker for increased risk of cardiovascular disease and diabetes is unresolved.

One has to understand that the metabolic syndrome definition is still evolving and would constantly do so as more and more data comes in. Furthermore, there is no reason to expect that there should be consensus on the definitions as each definition

was developed to correct the previous definitions, thus it would be unlikely that they would basically be similar.

At the same time, if one sees the timeline of the various definitions, it becomes clear that we are moving towards some sort of a consensus on what defines the metabolic syndrome as shown (Table 1).

Table 1. Previous criteria proposed for the diagnosis of metabolic syndrome

Clinical measure	WHO (1998)	EGIR	ATP III (2001)	AACE (2003)	IDF (2005)
Insulin resistance	IGT, IFG, T2DM, or lowered insulin sensitivity plus any 2 of the following	Plasma insulin >75th percentile plus any 2 of the following	None, but any 3 of the following 5 features	IGT or IFG plus any of the following based on clinical judgment	None
Body weight	Men: waist-to-hip ratio >0.90; women: waist-to-hip ratio >0.85 and/or BMI >30 kg/m^2	WC ≥94 cm in men or ≥80 cm in women	WC ≥102 cm in men or ≥88 cm in women	BMI ≥25 kg/m^2	Increased WC (population specific) plus any 2 of the following
Lipid	TG ≥150 mg/dl (1.7 mmol/l) and/or	TG ≥150 mg/dl (1.7 mmol/l) and/or	TG ≥150 mg/dl (1.7 mmol/l)	TG ≥150 mg/dl (1.7 mmol/l)and	TG ≥150 mg/dl (1.7 mmol/l) or on TG Rx
	HDL-C <35 mg/dl (0.90 mmol/l) in men or <39 mg/dl (1.01 mmol/l) in women	HDL-C <39 mg/dl (1.01 mmol/l) in men or women	HDL-C <40 mg/dl (1.03 mmol/l) in men or <50 mg/dl (1.29 mmol/l) in women	HDL-C <40 mg/dl (1.03 mmol/l) in men or <50 mg/dl (1.29 mmol/l) in women	HDL-C <40 mg/dl (1.03 mmol/l) in men or <50 mg/dl (1.29 mmol/l) in women or on HDL-C Rx
Blood pressure	≥140/90 mmHg	≥140/90 mmHg or on hypertension Rx	≥130/85 mmHg	≥130/85 mmHg	≥130 mmHg systolic or ≥85 mmHg diastolic or on hypertension Rx
Glucose	IGT, IFG, or T2DM	IGT or IFG (but not diabetes)	>110 mg/dl (6.1 mmol/l) (includes diabetes)[a]	IGT or IFG (but not diabetes)	≥100 mg/dl (5.6 mmol/l) (includes diabetes)
Other	Microalbuminuria			Other features of insulin resistance[b]	

[a] The 2001 definition identified fasting plasma glucose of ≥110 mg/dl (6.1 mmol/l) as elevated. This was modified in 2004 to be ≥100 mg/dl (5.6 mmol/l), in accordance with the American Diabetes Association's updated definition of IFG.
[b] Includes family history of type 2 diabetes mellitus, polycystic ovary syndrome, sedentary lifestyle, advancing age, and ethnic groups susceptible to type 2 diabetes mellitus.

It is quite possible that further changes may be made to the definitions as more data comes in from all over the world. After all, it is essential that we take a global view of the risks involved and the criteria may need to be changed in order to be inclusive and take into consideration the ethno-heterogeneity of the so called global village! This is definitely not a case where one size fits all, but one that requires needs to be "made to fit" so that it can have global clinical relevance.

An example of ethno-heterogeneity was the case of Asian Indians, who have been found to be at greater risk to obesity and insulin resistance than Caucasians, and researchers felt that the BMI cut-off should be decreased to <23 kg/m2 rather than <25 kg/m2 which was used as normal. This was accepted and different BMI cut –off have been defined for Asians. If that is the case, it might also appear that the uniformity and consensus in terms of the definition of metabolic syndrome is further questioned. But, it should rather appear that the consensus lies in appreciating the lack of uniformity of a universal definition and being sensitive to ethno-heterogeneity of risk factors.
Reaven stated in a recent report that it appears that studies demonstrating the relationship between increased abdominal obesity and adverse clinical consequences have relied on at least 14 different methods to quantify waist circumference (WC) and even the 4 most commonly used approaches yielded quite different absolute values for WC (53,54). This issue is further highlighted by a recent report from the WHO expressing concern that since the untoward effects of obesity will vary in different ethnic groups, it will be necessary to develop ethnicity-specific values to identify overweight/obese individuals at greatest risk (55).
The good news is that some of these criticisms have already been clarified by the updated NCEP and the IDF definitions which are the latest versions of the definition. It appears that we are moving towards a consensus definition of sorts as shown in table 2 (48,49).

Table 2. IDF and AHA/NHLBI

Comparison of diagnostic criteria for the metabolic syndrome from the International Diabetes Federation (IDF) and American Heart Association (AHA)/National Heart, Lung, and Blood Institute (NHLBI)

IDF clinical criteria for metabolic syndrome		**AHA/NHLBI diagnostic criteria for metabolic syndrome**	
Measure (central obesity plus any two of five other criteria constitute a diagnosis of metabolic syndrome)	**Categorical cut points**	**Measure (any three of the five criteria below constitute a diagnosis of metabolic syndrome)**	**Categorical cut points**
Central obesity	Waist circumference ethnicity specific For South Asians: ≥ 90 cm in men, ≥ 80 cm in women	Elevated waist circumference	General U.S. population: ≥102 cm (≥40 in.) in men, ≥88 cm (≥35 in.) in women; lower cut points for insulin-resistant individuals or ethnic groups (based on clinical judgment)
Raised triglycerides	>150 mg/dl (1.7 mmol/l) or on specific treatment for this lipid disorder	Elevated triglycerides	≥150 mg/dl (1.7 mmol/l) or on drug treatment for elevated triglycerides
Reduced HDL cholesterol	<40 mg/dl (1.03 mmol/l) in men, <50 mg/dl (1.29 mmol/l) in women or on specific treatment for this lipid abnormality	Reduced HDL cholesterol	<40 mg/dl (1.03 mmol/l) in men, <50 mg/dl (1.29 mmol/l) in women
Raised blood pressure	≥130 mmHg systolic blood pressure or ≥85 mmHg diastolic blood pressure or on treatment for previously diagnosed hypertension	Elevated blood pressure	≥130 mmHg systolic blood pressure or ≥85 mmHg diastolic blood pressure or on drug treatment for hypertension
Raised fasting glucose	Fasting plasma glucose ≥100 mg/dl (5.6 mmol/l) or previously diagnosed type 2 diabetes		

Studies have shown that the presence of the metabolic syndrome confers a two-fold increase in the risk for major CVD events and a five-fold increase in the life-time risk for T2DM [56 - 58). Although the precise increase in the risk may vary depending on the population being studied, from a clinical viewpoint the presence of the metabolic

syndrome identifies a person at higher lifetime risk for major CVD events and/or T2DM (57).

One has to realize that almost 200 million people globally have diabetes and 80% of these will die from cardiovascular disease. Thus it seems that the reason for the IDF for coming out with these clinically simple to use guidelines was the firm belief that we are in the midst of a twin pandemic of T2DM and cardiovascular disease which seems to be driven by the metabolic syndrome and the presence of the associated correlates in the metabolic syndrome confers a manifold increase in the risk for T2DM and CVD (56). Taking a global view, it becomes not only a medical, but also a socio-economic need to take all steps to try and prevent the ravages which can be caused by T2DM and CVD (2).

The risk factors underlying cardiovascular disease can be divided into (59);

(a) Major risk factors, such as cigarette smoking, elevated LDL-C and VLDL-C, low HDL-C, elevated blood pressure, diabetes, metabolic syndrome and advanced atherosclerotic burden.

(b) Emerging risk factors being, prothrombotic stage, proinflammatory state, insulin resistance

(c) Underlying risk factors being atherogenic diet, obesity, physical inactivity & family history.

1.2.3 Epidemiology of the Metabolic Syndrome

The widespread use of the different metabolic syndrome definitions has resulted in a large number of publications describing varied levels of prevalence of the disease. The NCEP criteria have been used in a broad spectrum of cases; HIV subjects, American indigenous population and in representative surveys of many countries (60–64). The prevalence of the NCEP-metabolic syndrome in the U.S. was initially reported in the Third National Health and Nutrition Examination Survey (NHANES III, 1988–1994). The age-adjusted prevalence was 23.7% (62). The contribution of the various components was different among ethnic groups. Low HDL cholesterol, hyperglycemia and hyper-triglyceridemia made a significantly greater contribution in Mexican-Americans compared to arterial hypertension which was more prevalent in African-Americans.

The prevalence of the NCEP-metabolic syndrome was updated in the U.S. using the NHANES 1999–2000. The age-adjusted prevalence increased from 24.1 to 27% (63).

Remarkably, an increased prevalence was observed mainly in women younger than 40 years of age. These results are a worrisome indicator of future trends in diabetes and CVD in the U.S as well as showing where trends are going globally.

The WHO criteria have been used mainly in European cohorts (61). The prevalence of the WHO-metabolic syndrome in non-diabetic subjects varied between 7 and 36% for men 40–55 years and between 5 and 22% for women of the same age group. The same trends were observed if patients with or without diabetes were included in the analysis.

Analyses of data from large, prospective studies suggest that the metabolic syndrome itself is an important risk factor for CHD and type 2 DM, and that the metabolic syndrome increases total mortality and cardiovascular mortality (58).

The Botnia study followed individuals from families with type 2 DM in Finland and Sweden (65). According to an analysis of 4483 subjects aged 35–70 years, the prevalence of the metabolic syndrome according to WHO criteria increased in a stepwise fashion with worsening glucose tolerance. Over a median follow-up period of 7 years, the presence of the metabolic syndrome tripled the risk of CHD and doubled the risk of myocardial infarction and stroke. The risk of cardiovascular mortality was 80% greater in subjects with the metabolic syndrome than in those without, and the risk of all-cause mortality was also significantly greater.

A12-year follow-up data was examined from a Finnish study of 2682 middle-aged men who did not have cardiovascular disease or diabetes at baseline (66). Death from CHD was 2.9–4.2 times more likely among men with the metabolic syndrome than among those without, depending on how the syndrome was defined. In addition, the presence of the metabolic syndrome doubled the risk of death from any cause.

Associations between the metabolic syndrome, CHD, and diabetes have also been established by an analysis of the cross-sectional NHANES III data on adults aged >50 years (67). As in the Botnia study, a stepwise increase in the prevalence of the metabolic syndrome was observed with worsening glucose tolerance, and 86% of people with diabetes had the metabolic syndrome (65). The prevalence of CHD was 19% in people with both the metabolic syndrome and diabetes versus 9% in those with neither and 7.5% in the small percentage of the study population that had diabetes but not the metabolic syndrome. These results suggest that for most diabetic patients, cardiovascular risk is related not to diabetes itself but to the concomitant presence of the metabolic syndrome (68).

Currently available definitions are extremely valuable tools for studying the disease. However the current definitions include, in affected and non-affected subjects a heterogeneous group of cases with a broad range of relative risks for future complications, which need to be refined. The refinement of the definitions will allow the correct identification of cases and controls for genetic studies, the method most likely to provide the gold standard for the diagnosis of the syndrome (69).
Finally, the metabolic syndrome should be considered as a prime target for preventive medicine. Clearly, the emerging global epidemic of metabolic and vascular disease has significant implications for the development of population health promotion strategies. Lifestyle modifications and weight loss programs are a key part of the program because weight loss reduces the incidence of type 2 diabetes and a large percent of the affected subjects had excess body weight (70). However, long-term efficacy of the weight loss programs is far from ideal. Unless preventive programs are properly designed and implemented, we will continue to treat the majority of the cases when they have reached the steeper extreme of the road: when many have already developed the complications of the metabolic syndrome.

1.2.4 Metabolic Syndrome in South Asians

In the future 70% of new incident cases of diabetes will be in the developing countries (71). Among the ten leading countries with diabetes, five are in Asia (72-73). In 2025, India will rank first with 57 million diabetics, followed by China in second place with 38 million diabetics and Pakistan in 4th place with 14.5 million diabetics (74).

Table 3. Top Ten Countries for Number of Persons with Diabetes

(WHO estimates, 1995-2025)

	(1995)		(2025)	
	Country	millions	Country	millions
1	India	19.4	India	57.2
2	China	16.0	China	37.6
3	U.S.A.	13.9	U.S.A.	21.9
4	Russian Fed.	08.9	Pakistan	14.5
5	Japan	06.3	Indonesia	12.4
6	Brazil	04.9	Russian Fed.	12.2
7	Indonesia	04.5	Mexico	11.7
8	Pakistan	04.3	Brazil	11.6
9	Mexico	03.8	Egypt	08.8
10	Ukraine	03.6	Japan	08.5

South Asian (SA) refers to people who originate from India, Sri Lanka, Bangladesh, Nepal, Maldives and Pakistan (75). South Asian migrant populations have a two to three fold higher prevalence of diabetes than their Europeans counterparts (76). South Asians are particularly predisposed to develop diabetes mellitus and coronary heart disease (CHD) (28, 77-79). This is mainly due to the fact that South Asians are consistent more insulin resistance as shown in various studies (80-82). Important and consistent observations related to high prevalence of insulin resistance in South Asians show presence of excess body fat and abdominal obesity (83). Although South Asians have a lower BMI, they have a higher fat content and more subcutaneous fat (84,85)

Obesity is a very most important factor associated with insulin resistance. Increase of 1/3rd over ideal body weight decreases insulin sensitivity by 40% (86). However it is important to note that all obese individuals are not insulin resistant. Obesity is also frequently associated with insulin resistance in South Asians settled in other countries as well in India (87-91).

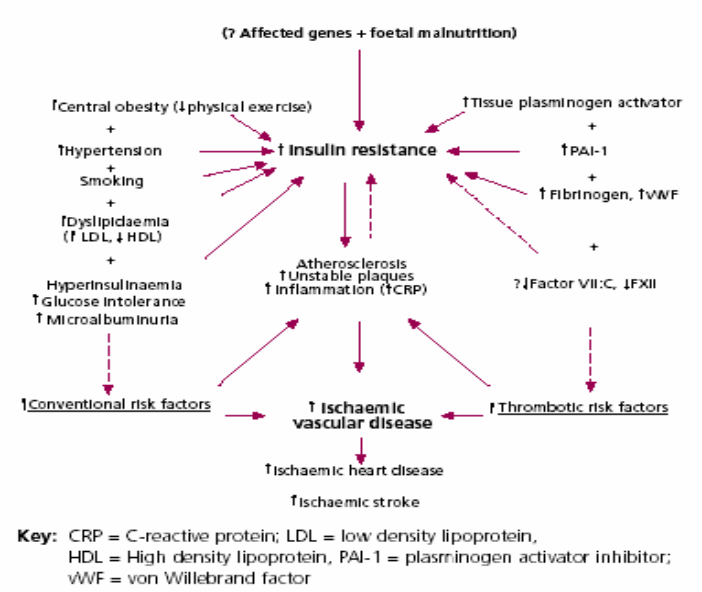


Figure 2: Features of Metabolic Syndrome / Insulin Resistance in South Asians

Overall, the prevalence of insulin resistance in South Asians (5–50%) is reported to be highly variable. This could be due to different methodologies employed by various scientists for the assessment of insulin resistance such as Reaven who emphasized that the metabolic syndrome was just a small part of the all encompassing insulin resistance and the two terms could not be used interchangeably (82). Moreover, tremendous heterogeneity of South Asians in terms of their geographical location and partial adaptation of lifestyle of the country of residence, in addition to variations due to age, gender, and socio-economic strata may also contribute to this variation in prevalence of metabolic syndrome.

The purpose of making a diagnosis of the metabolic syndrome is to initiate and implement lifestyle changes so as to decrease the risk of CVD. Since 15–16% of global mortality due to CVD is contributed by India this approach could make a significant difference in South Asians to reduce the risk of CVD (92). Although a specific risk factor influences the risk that a person will have cardiovascular disease, risk factors tend to aggregate and usually appear in combination (79).

Epidemiological studies have established that multiple risk factors increase the probability of cardiovascular morbidity and mortality in a multiplicative fashion. We already know that high prevalence of CHD has been observed in immigrant South Asians (93-95). What is particularly important in South Asians is that the three classical risk factors for CHD – smoking, hypertension and hyper-cholesterolaemia – fail to explain the high levels of Coronary Heart Disease (96-97).

Thus comes the role of insulin resistance as suggested in the study done in South Asians (Indian and Pakistani subjects) living in London. This study demonstrated that despite being matched for age and body mass index (BMI) with Caucasians, South Asian men had higher waist: hip ratio, higher systolic blood pressure (BP), higher insulin levels after glucose load, higher triglyceride levels and lower high density lipoprotein (HDL)-levels, all suggesting a high prevalence of the Metabolic Syndrome. Thus the CHD risk factors tend to aggregate in those with the metabolic syndrome. In addition, type 2 diabetes a CHD risk equivalent was prevalent in 20% of the South Asians compared with 5% of Caucasians adding to the CVD risk burden (98).

1.3 Pakistan – Country Profile

Pakistan is a poor and underdeveloped country, however government policies since 2001, bolstered by generous foreign assistance and renewed access to global markets have generated macroeconomic recovery in the last five years. The government has made substantial macroeconomic reforms since 2000. Poverty levels have decreased by 10% since 2001. A brief overview of the country is given below:

1.3.1 Geography:

The country is located in Southern Asia, bordering the Arabian Sea, between India on the east and Iran and Afghanistan on the west and China in the north. Geographic coordinates are 30 00 North and 70 00 East. Total land boundaries area with countries is 6,774 km; Afghanistan 2,430 km, China 523 km, India 2,912 km, Iran 909 km while the coastline is 1,046 km.
Total area is 803,940 sq km of which land is 778,720 sq km & water is 25,220 sq km.

1.3.2 People:

Population is estimated to be 164,741,000 as of 2007.
The five main ethnic groups are Punjabi, Sindhi, Pashtun (Pathan), Baloch and Muhajir (immigrants from India at the time of partition and their descendants).
Languages:
Punjabi 48%, Sindhi 12%, Siraiki (a Punjabi variant) 10%, Pashtu 8%, Urdu (official) 8%, Balochi 3%, Hindko 2%, Brahui 1%, English (official; lingua franca of Pakistani elite and most government ministries), Burushaski and other 8%,

Estimates from CIA World Fact Book

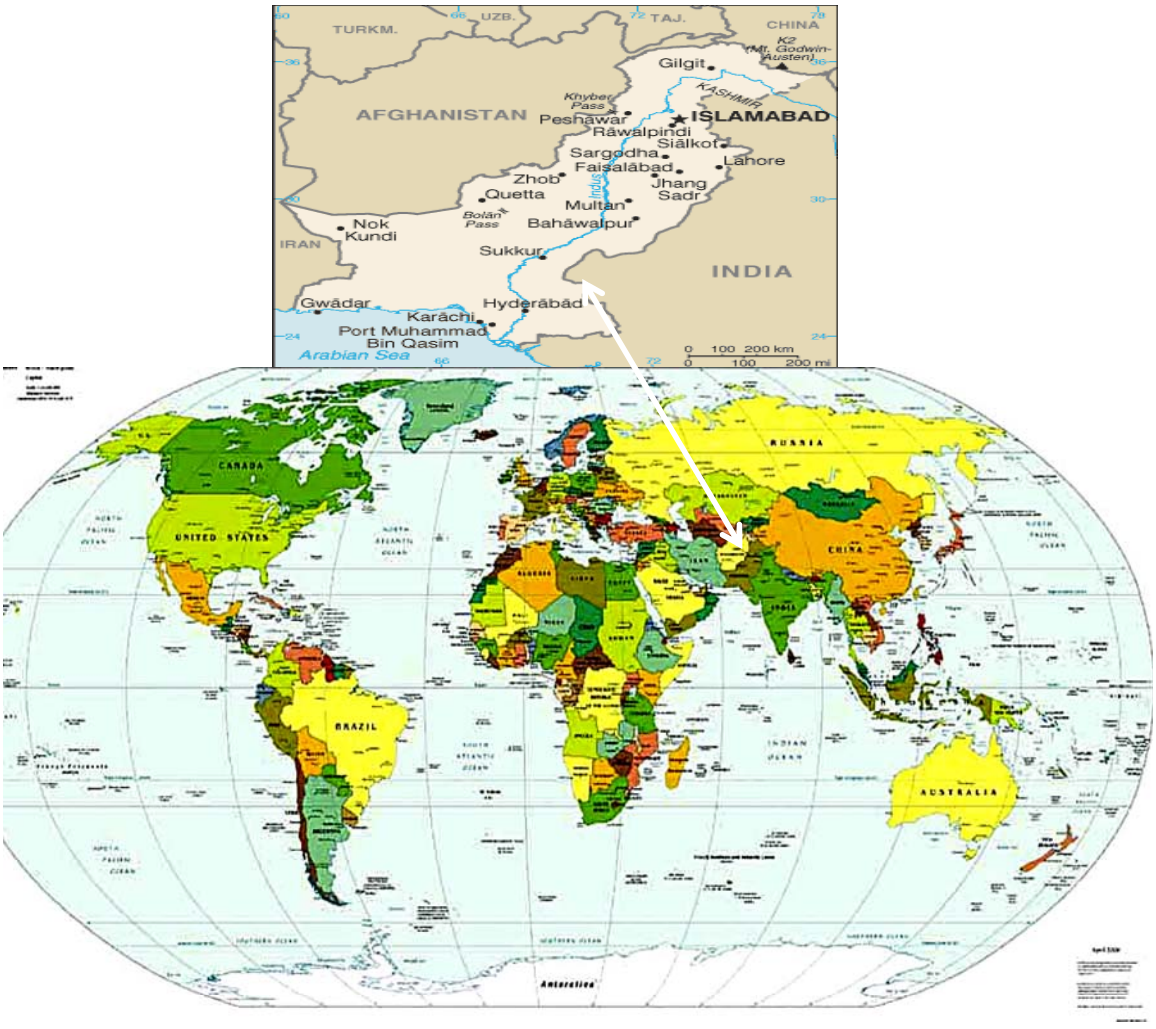


Figure 3 : Geographic Location of Pakistan

1.3.3 Population Demography:

Thirty seven percent of the country's population is less than 14 years of age. Around 58.8% of the population is between 15-64 years while 4.3% of the population is 65 years or above. The overall median age is around 20.9 years while it is 20.7 years for males and 21 years for females.

Sex ratio is 1.045 male(s)/female for the total population.

Population growth rate: 1.828%

Birth rate: 27.52 births/1,000 population

Death rate: 8 deaths/1,000 population

Life expectancy at birth for the total population is 63.75 years. It is 62.73 years for males and 64.83 years for females.

1.3.4 Education

Education in Pakistan is mostly subsidized by the Government from primary schools to higher education levels in public universities. The definition of literacy is taken as over 15 years of age and able to read and write. This level of literacy for the total population is 48.7% while it is 61.7% for males and 35.2% for females according to 2004 estimates.

1.3.5 Economy

Pakistan's economy depends mostly on agriculture. The GDP - per capita (PPP) of the country is $2,600 according to 2006 estimates. Unemployment rate is 6.5% plus substantial underemployment while 24% of the population lives below poverty line. Poverty line is the minimum level of income deemed necessary to achieve an adequate standard of living. Definition of poverty varies considerably amongst nations and the definition of poverty line is significantly higher in developed nations than in developing nations. Here it is taken as one US dollar.

1.3.6 Lifestyle and Physical Activity

Lifestyle of the people is different according to rural and urban settings. Apart from household work the women in the rural areas also help their men in the fields and in looking after cattle. Compared to this the people in city are exposed to a easier way of daily life. Pakistani people do not have a tradition of doing extra physical exercise apart from the requirements of their daily work.

1.3.7 Diabetes in Pakistan

The World Health Organization estimated that there would be approximately 5.2 million diabetics in Pakistan in the year 2000, ranking it at sixth place among countries with the highest number of diabetics (74). The current scenario is that there are 6.9 million diabetics in Pakistan according to International Diabetes Federation (31). This number is predicted to increase to 14.5 million by the year 2025-2030 (31, 74). The predictions are modeled upon the reported prevalence of T2DM in the national survey conducted by the Diabetic Association of Pakistan (DAP) in collaboration with the World Health Organization (WHO) during the 1990s (99-101).

Conducted in urban and rural areas in the four provinces (NWFP, Baluchistan, Punjab and Sindh), the national survey used WHO guidelines for the diagnosis of T2DM and impaired glucose tolerance (IGT) in over 5,600 persons 25 years and older. The overall prevalence of T2DM among men and women was reported as 11%, with overall abnormal glucose control of 22%. A summary of the results is given in table 4 below. A higher prevalence of obesity and IGT was observed among women as opposed to men and a relatively higher prevalence of diabetes and IGT was found in younger age groups (99-101) as compared to western populations. Nearly half of the subjects in these surveys did not know they had diabetes.

Table 4. Pakistan National Diabetes Survey

Province		Diabetes(%)	IGT(%)
Sindh	(Rural)	13.9	11.2
	(Urban)	16.5	10.4
Baluchistan	(Rural)	07.5	07.4
	(Urban)	10.8	10.4
NWFP	(Rural)	12.0	09.4
Punjab	(Rural)	06.2	05.6
	(Urban)	13.7	10.3
Overall		11.5	9.3

1.3.8 CVD in Pakistan

Data on CVD in Pakistan is sparse, with a few hospital-based descriptive studies providing the only estimates of CVD available. One such study on acute myocardial infarction (AMI) based on admissions to two tertiary care centers in Lahore and Sheikhupura over a one year period ending in 1993 concluded that the prevalence of symptomatic IHD in younger age group (< 35 years) is about 4% in Lahore and about 6% in Sheikhupura (102).

Risk Factors Associated with CVD

These risk factors can be classified into two categories:

1 Those that have been proven to be causal (risk factors). These markers could be classified as predisposing (e.g., obesity which may work through raising blood pressure, glucose, and lipids) or direct (e.g., smoking).(103)

2 Those that have shown association with CHD but for whom a cause and effect association is yet to be proven (risk markers).(103)

Table 5. Risk Factors that are causally linked

1. Tobacco consumption
2. Elevated LDL
3. Low HDL
4. High Blood Pressure
5. Elevated glucose
6. Family history
7. Physical inactivity*
8. Obesity*

Table 6. Risk markers that show associations:

1. Low socioeconomic status*
2. Elevated prothrombotic factors: fibrinogen, PAI-1
3. Markers of infection or inflammation
4. Elevated homocysteine
5. Elevated lipoprotein (a)
6. Psychological factors (depression, anger proneness, hostility, stress, acute life-events) and breakdown in social structure (loss of social support and cohesion)*

* Predisposing risk factors: A predisposing risk factor is presumed to work, at least in part, through an impact on other risk factors that act directly.
PAI indicates Plasminogen activator inhibitor.
(Adopted from Global Burden of Cardiovascular Diseases - 103)

1.4 Statement of Problem

In view of the increasing prevalence of type 2 diabetes in Pakistan, it is reasonable to postulate that there is a increasing epidemic of metabolic syndrome going on in Pakistan at the moment. Since the metabolic syndrome is a long-term process that starts early in life and is involved in the patho- physiology of type 2 diabetes and atherosclerosis, vigorous early management of the syndrome will have a significant impact on the prevention of both diabetes and CVD (3,5,85–87).

A study done in 400 cardiac patients at a tertiary cardiology unit in Pakistan according to ATP III definition showed a prevalence of 44% metabolic syndrome (104). While in another study done in type 2 diabetic subjects in Karachi, subjects had 46% metabolic syndrome according to the WHO definition (105).
Epidemiological studies have demonstrated the associations between these risk factors with the twin epidemic of T2DM and CVD.
Community-based interventions to reduce these risk factors have proven effective in developed countries for preventing T2DM and CVD, with a limited number of studies in developing countries indicating that similar gains are potentially achievable here as well. Diabetes prevention and control is particularly relevant in Pakistan; increased inherent predisposition, younger age of onset, lack of capacity to effectively treat the condition at the primary healthcare level and lack of equitable access to healthcare for possible complications makes a strong case for investment in diabetes prevention and control (106-107).
The awareness of ethnicity as a potential independent risk factor for chronic disease has clinical importance since lower thresholds would have to be considered for primary prevention strategies in certain ethnic groups (83,84). The current study will establish baseline values for insulin levels and assess the prevalence of metabolic syndrome among adults in urban Karachi and lay the foundations for future intervention studies of primary prevention of Type 2 diabetes and CVD.

1.5 Research Questions and Objectives of the Study

1.5.1 Research Questions

1. What is the prevalence of metabolic syndrome based upon WHO, ACE, EGIR, modified ATP III and IDF definition in this Pakistani population?

2. What is the prevalence of diabetes and other forms of abnormal glucose tolerance in subjects aged 25 years and above in Karachi, Pakistan?

3. What is the distribution and relationships of cardiovascular disease and its risk factors in this population with metabolic syndrome?

4. What is the insulin resistance for our population?

1.5.2 Main Objective

- ✓ To determine the prevalence of metabolic syndrome in a sample of adults aged 25 years and above from an urban population of Karachi.

1.5.3 Specific Objectives

More specifically, the objectives of the study were to:

- ➢ Estimate and compare the differences in prevalence of metabolic syndrome based upon WHO, ACE, EGIR, modified ATP III and IDF definition in Pakistani population.

- ➢ Estimate the prevalence of diabetes and other forms of abnormal glucose tolerance and association of IFG with metabolic syndrome.

- ➢ Assess the distribution and relationships of cardiovascular disease and its risk factors with metabolic syndrome.

1.6 Justification of the Study

- It is recognized that the features of the Metabolic Syndrome can be present up to 10 years preceding Type 2 diabetes and CVD (88). The driving force behind high diabetes and CVD incidence in South Asians could be having the Metabolic Syndrome.

- The rising prevalence of obesity and metabolic syndrome has received increased attention in recent years since both place individuals at risk for Type 2 diabetes and CVD. The detection of conventional risk factors associated with Metabolic Syndrome is important for primary prevention programs for diabetes and CVD.

- The combination of the components of the metabolic syndrome may give the epidemiologist an instrument with a good predictive power for future diabetes and CVD detection.

- The metabolic syndrome may also provide the primary care physician an integrative view linking conditions frequently seen together but thought unrelated in the past such as hypertension and low high-density lipoprotein cholesterol.

- Thus, the metabolic syndrome could possibly be a fundamental part of the public health policy as prospective data have shown that treatment of its components delays or prevents occurrence of disease.

Chapter 2: Material and Methods

2.1 Scope of study

This study was designed as a prevalence survey for metabolic syndrome among 500 randomly selected households in Lyari. We also assessed the prevalence of diabetes and cardiovascular disease in this population.

2.2 Research Setting

Lyari is one of the oldest and most densely populated part of Karachi city (estimated population of 13-14 million in 2004). Lyari's approximately 700,000 residents form an extremely diverse community, representing almost every cultural and ethnic groups found in Pakistan. The area was originally inhabited by Baluchi tribes that moved here from around the Makran coast during the 18th century, joined soon thereafter by Sindhi tribes from around the Indus river and delta. Large migrant communities from Gujrat and Bihar first settled in Lyari following the partition of British India. Economic migrants, mostly men, from the Punjab and North West Frontier Province (NWFP) arrived during the 60s and 70s, followed by refugees from the war in Afghanistan during the 80s. These migrants have gradually brought their families to settle here as well. Significant Christian and Hindu neighbourhoods are scattered in between the majority Muslim population. There is similarly a wide spectrum of socioeconomic groups.

2.3 Lyari Town Geographical Information System

Lyari Town Geographical Information System was made by Population Census Office, Statistics Bureau Sindh, National Database and Registration Authority (NADRA) and Interactive Research and Development, a private research organization to define the geopolitical boundaries and population density of Lyari Town (estimated 2004 population of 700,000). This was done by dynamically linking the national census database to a purpose built geographical information system (GIS). A year-long, detailed physical survey of Lyari Town was then undertaken using available plot maps, most of which were over 20 years old. Although these plot maps required extensive and careful updating, the final results of the physical survey were impressive; all household structures were given a unique identification number, along with all health, education and other civic facilities available to its residents. The edited plot maps were then newly traced, with the unique number ascribed to each

household clearly visible and commercial and civic services clearly high-lighted. The new maps were finally digitized using a geo-referenced satellite image of Lyari town at 1 meter resolution as shown in figure 4. The objective of developing the Lyari Town GIS has been to lay the infrastructure for the longitudinal follow-up of households to assess indicators that may be of interest to researchers, including determining the community-based prevalence of chronic diseases among adults as has been done by our group.

Lyari Town: Population 699,595
Ikonos 1 m Resolution; Vector Referenced ±10 ft

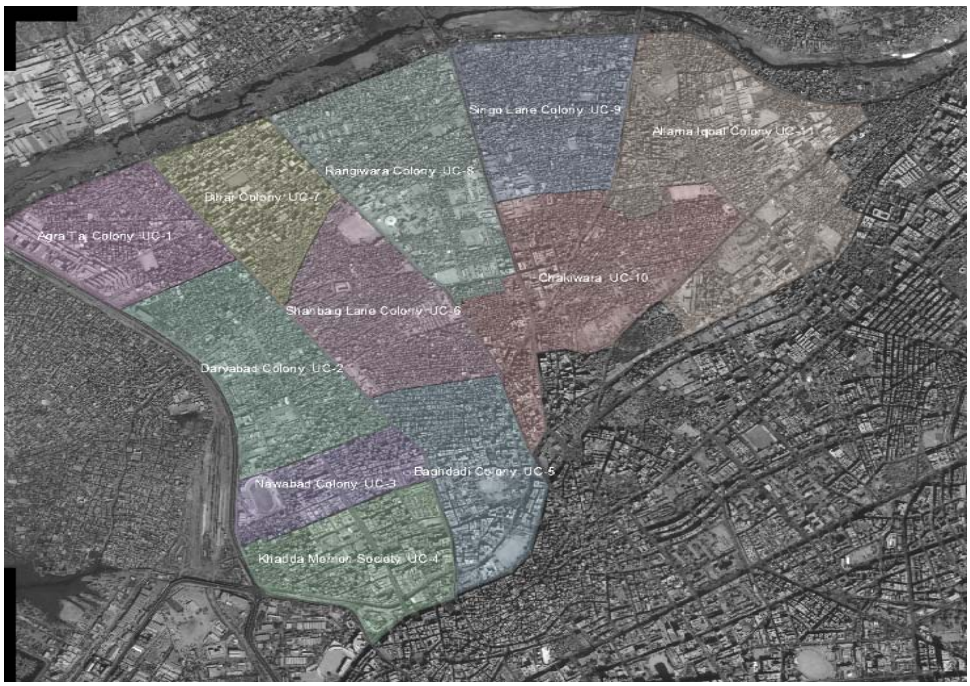


Figure 4: Lyari Town

Lyari Town: 85,520 Households
500 Households Randomly Selected

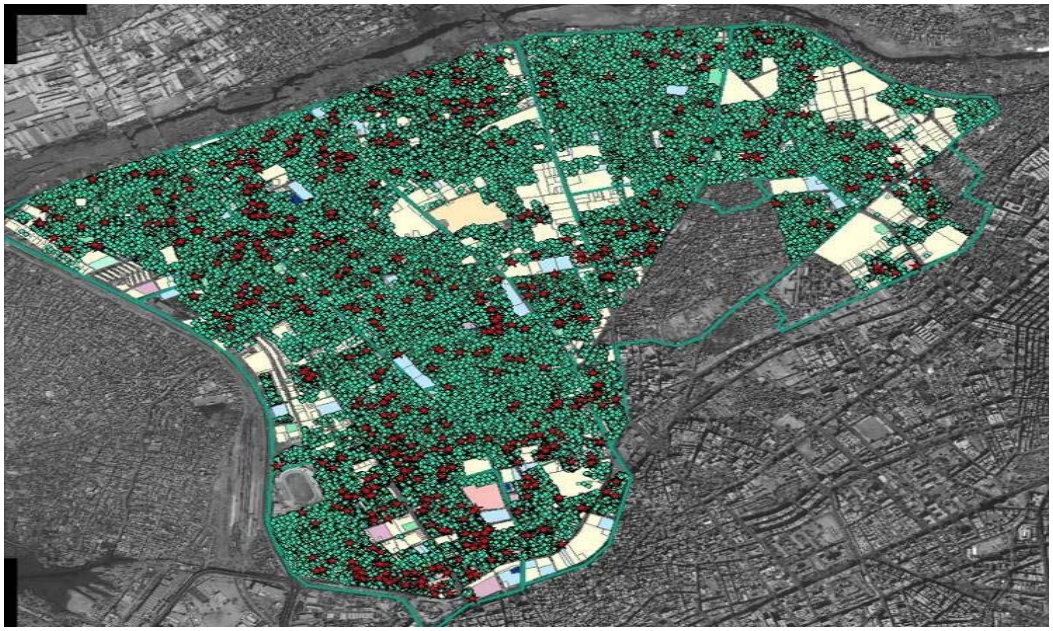


Figure 5: Randomly Selected 500 Households

2.4 Study Population

We generated a computerized random sample of 500 households from among the 85,520 households in Lyari Town as shown in figure 5. There were 11 union councils or subdivisions of Lyari Town where the samples were taken from ensuring that each union council had equal opportunity to be represented in the sample selection. We expected approximately 1000 adult men and women 25 years and above in the 500 households in Lyari. If members of a household that had been selected refused to consent to household interviews, we knocked on the third door to the right of that house (while standing facing the door of the original house) and seeked consent there. If we were refused again, we knocked on the next consecutive door to the right and repeated this process until we had enrolled a household from the neighbourhood of the original household selected.

Individual members within households also reserve the right to refuse participation in the study. Assuming a 10% refusal rate (by members within the household at the time of interview) and another 10% refusal rate by those who decline to provide consent for a blood test, we expected at least 810 individuals to participate in this study.

2.5 Criteria for Inclusion and Exclusion

- All adults 25 years and above from the households selected and who gave their informed consented were included in the study.

- Persons with physical or intellectual disabilities that precluded participation in the study were not included.

- Those were also excluded who had resided in the current address for less than 6 months prior to the survey.

2.6 Sample Size

In planning phase the following assumption was made by the research group;

1) Assuming that the prevalence of T2DM to be 11% in this population (prevalence in urban populations is actually higher),
2) the size of the population from which the study sample is to be selected (persons 25 years and above in Lyari Town) is 244,000,
3) the worst acceptable result is ±1.5% from the true population value, our study would require a sample of at least 713 individuals to have 80% power to detect the true population value.
4) Since the prevalence of metabolic syndrome is assumed to be higher than that of diabetes we believe this sample size would be sufficient for assessing metabolic syndrome in our population.

In the field we were able to interview 867 individuals; more than the required number but only 363 individuals gave blood samples leaving us with less than the required numbers at the end of the study giving us 40 – 45% power to detect true population value.

2.7 Research Design

2.7.1 Survey protocol and procedures

The survey activities were conducted over a period of 6 months from July to December 2004. A Geographical Imaging Systems (GIS) as already described,

previously developed for Lyari Town with unique identification numbers ascribed to 85,520 households was used.

The survey activities were divided into two phases—the household interview plus physical examination and blood sample collection.

A household was defined as including all those who shared a kitchen. Five hundred households were randomly selected through the GIS software and maps to these households were generated for 9 field teams. A field team comprised of one or two medical students, a female health worker and a male health worker. Surveyors from the GIS teams worked as guides for 2-3 teams in a given area. All teams and surveyors were supervised by a medical doctor acting as the field coordinator.

2.7.2 Household census and interview

Twelve medical students conducted these household visits with assistance from 8 health workers from Lyari Community Development Project – a local welfare organization. Once a household was located, medical students identified themselves to the oldest male or female member present and informed them of the objectives of the survey. All adults 25 years and older were invited to participate after providing signed consent. In case of illiterate participants, the consent form was read out to them and a thumb print procured in the presence of a household member or neighbour as witness.

Field work entailed afternoon visits to the selected household by a field team (medical students and health worker), introduction to the purpose of the research study, consent, interviews and physical measurements (including weight, height, waist and hip circumference, blood pressure).

The interviewers made a minimum of 2 visits and up to 5 visits before a household was classified as a non contact. Where possible, at each participating household a personal interview was conducted with every adult member aged 25 years and above who met the eligibility requirements.

At the end of the household visit, all adults 25 years and above were asked to undertake an 8 hour fast for blood tests (fasting blood sugar and lipid profile) that was collected at home on Saturday and Sunday mornings. All adults were provided with a urine collection bottle and asked to collect a mid-stream urine specimen for tests (pus cells, proteinuria and microalbuminuria) on the morning of their blood test date.

2.7.3 Questionnaire

The adults present in each household were administered a survey form (Questionnaire) which consisted of 3 main parts (Appendix - 1).

a) Part A collected information about the entire household and was same for all the persons living in a specific household. It consisted of 4 sections.
b) Part B of the survey form collected information about personal and family history of the individual persons in each household and consisted of 6 sections. Part B of the survey form consisted of question forms in Urdu for easy understanding of the community.
c) Part C collected anthropometric information about the individual persons and also lab reports were written in this section.

1. **Part A**

It consisted of 4 sections and collected information about the entire household individuals.

Section A1 asked questions about household demography including total number of persons residing in the house, their relationship with head of household, ethnicity and place of birth etc.

Section A2 had 8 questions about the household diet with reference to fat, oil and salt intake.

Section A3 had 10 questions to assess the socioeconomic status.

Section A4 showed the morbidity and mortality of each household. This also included the type and cost of treatment as well as the number of deaths during the last 3 years.

2. **Part B**

It consisted of 6 sections and collected information from individual persons about personal and family history. It contained question forms in Urdu for easy understanding by the community.

Section B1 consisted of 24 questions in Urdu on personal demographics and personal medical history of each person interviewed.

Section B2 consisted of 16 questions about family medical history.

Section B3 contained 29 questions about tobacco consumption and smoking.

Section B4 had 40 questions about personal dietary habits with a list of commonly used food items.
Section B5 consisted of 9 questions on chest pain on physical exertion (Rose).
Section B6 had 8 questions about physical activity and exercise during the last 7 days.

3. **Part C**

Collected anthropometric data and included measurements of weight, height, waist and hip circumference. Participants were asked to wear light clothing and take off their shoes during anthropometry measurements. Height was measured to the nearest cm and weight to the nearest 0.1 Kg. Weight was taken with a standardized scale and height with a standardized measuring stick. Waist circumference was measured as the mid point between the iliac crest and the lower margin of the ribs. Blood pressure was take by a medical student or doctor at least twice with 20 minute intervals, after ensuring that at least 30 minutes had passed since tea or tobacco were last consumed. A third BP measurement was taken if one or both of the first two readings were above the cutoffs for a diagnosis of hypertension.

2.7.4 Blood Samples

Specimens were collected at home on Saturdays and Sundays by five mobile teams consisting of two phlebotomists each. At the time of blood collection on Saturdays and Sundays, all participants were asked to provide consent for blood tests for fasting blood glucose and lipid profile and urine for proteinuria. We also asked for consent for tests to be conducted on stored sera based on future research protocols, including genetic studies. Aliquots of serum from all participants were stored at -70 degrees Celsius for up to 5 years.
All blood samples were collected in two separate test tubes; a red caped vacutainer and green capped fluoride tube. A total of 12 cc of blood was taken from each patient. 10 cc was place in the vacutainer for analysis of Lipid profile and insulin serum levels and remaining 2cc was placed in the NaF test tube for analysis of fasting glucose.

Within 1 hour of collection the blood was centrifuged and separated; tests done by the Vitalab Selectra Analyzer for;

1. Glucose
2. Cholesterol
3. Triglycerides
4. HDL-Cholesterol
5. LDL-Cholesterol
6. Insulin

Fasting blood glucose and lipid profile were done by GOD PAP method and CHOD PAP method respectively. Insulin levels were done by Elisa method.

2.7.5 Urine Samples

This was collected by the respective subject on the morning of collection. They were advised to keep the specimen in a cool and shaded area. Urine tests included a qualitative determination of proteinuria and a quantitative measurement of microalbuminuria.

2.8 Statistical analysis

All data was recorded on forms developed using TeleForm® Version 6.01, an optical character recognition software. Forms were scanned, read and verified using TeleForm® Version 6.01 and exported into an SQL database. Later this data was converted into the software package SPSS version 11.5 (Statistical Package for Social Sciences) for analysis.

The main variables for analysis included age, gender, socioeconomic and ethnic groups, fasting glucose and insulin levels, lipid profile, proteinuria and microalbuminuria, hypertension, body mass index, waist-hip ratio, mid-abdominal circumference, smoking exposure and family history of disease. Some of the other risk factors to be included in the analysis were physical activity and diet.

We started with frequency analysis of all the variables in the survey form and cross-tabulation of the main variables. We estimated the odds of impaired glucose control, high risk lipid profiles, proteinuria, microalbuminuria, hypertension, high body mass index, high waist-hip ratio, large mid-abdominal circumference, smoking exposure

and family history of disease by age, gender and metabolic syndrome group, using chi square for categorical variables. In addition, difference in the means of continuous variables between these groups will be tested using the t-test or ANOVA.

2.9 Ethical Considerations

2.9.1 Ethical Clearance

The study protocol was approved by the institutional review board of the Baqai Institute of Diabetology and Endocrinology (BIDE) and by the Local Ethics Committee of the Lyari Community Development Project (LCDP).
The study protocol had also been sent to the Norwegian Ethics Committee for approval.

2.9.2 Informed Consent

Informed consent is a prerequisite for all research involving human subjects. Verbally and in writing, subjects were informed about the purpose and scope of the study, the benefits and risks of the study, how the results will be used and reported and the method of confidentiality that will be used in reports. Since all the subjects were interviewed from a structured questionnaire; questions did not probably change from subject to subject.
All participants were required to give their informed consent voluntarily and the study was carried out in accordance with the Declaration of Helsinki as revised in 2000. Participation for household interview and laboratory tests required the consent form to be signed in front of a witness. All participants reserved the right to withdraw from the study at any time, even if they have previously given consent to be part of study. The findings were treated with highest possible degree of confidentiality. Each subject was given a unique identity number.

Chapter 3: Results

3.1 Results

In this chapter descriptive analysis of the main variables present in the survey questionnaire will be presented followed by prevalence of glucose tolerance and distribution of cardiovascular disease risk. Secondly prevalence of the metabolic syndrome based on different definitions will be compared. Finally percentiles of insulin levels in the community will be defined.

3.1.1 Part A: Household Section of Questionnaire

The total number of households visited was 532 in which 3608 persons resided. Of these 51% were males while 49% were females. Out of these 3608 persons 1493 were ≥ 25 years of age. Of these 734 (49.2%) were males while 759 (50.8%) were females.

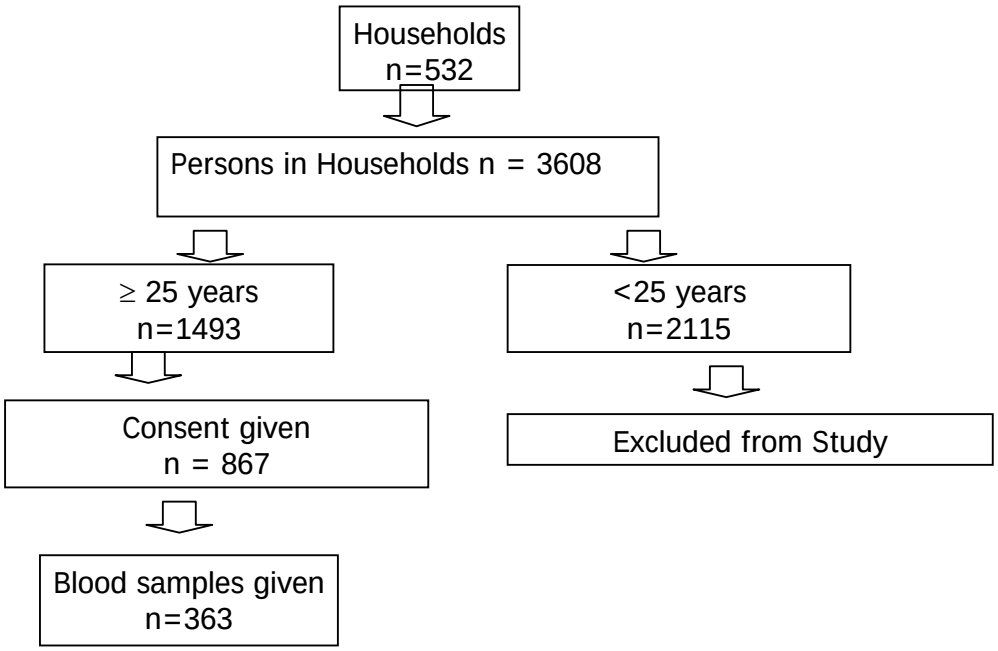
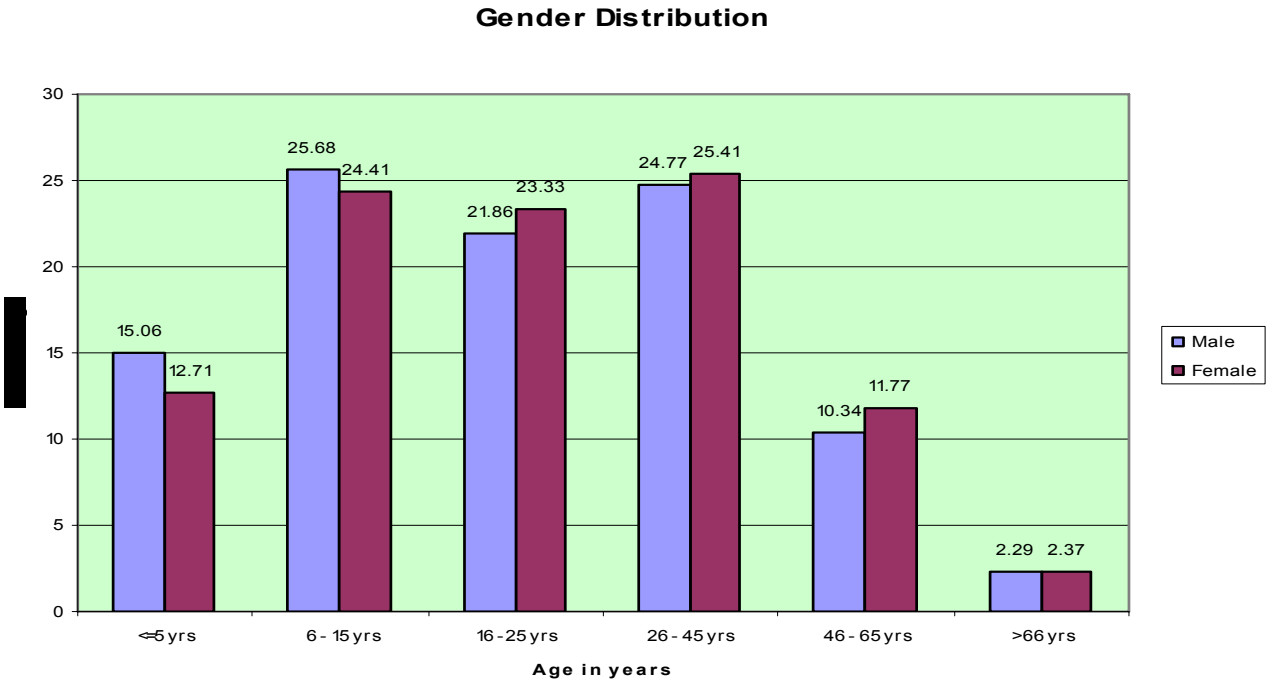


Figure 6: Household Survey – No of Eligible Persons

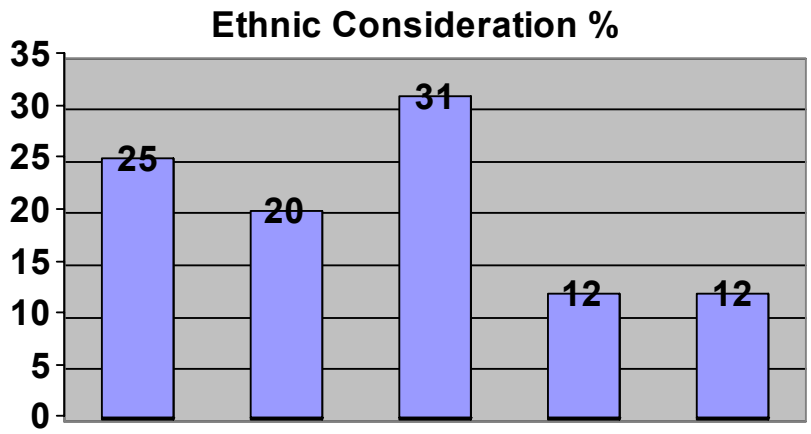
3.1.1.1 Section A1 asked questions about household demography including total number of persons residing in the house, their relationship with head of household, ethnicity and place of birth.

***Figure 7: Age and Gender distribution of Sample* (n=3608)**



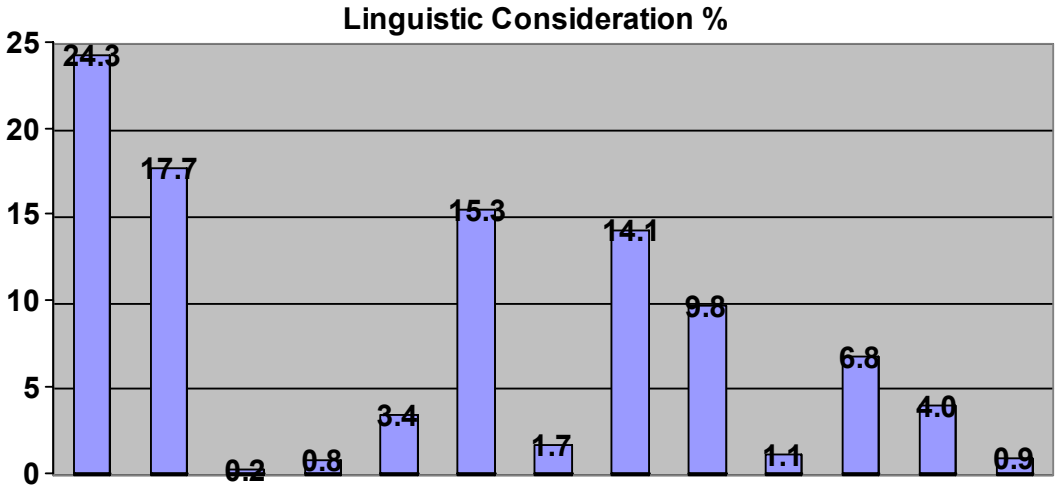
Looking at the ages of the persons residing in these 532 households a total of 154 children were less than 1 year of age.

***Figure 8: Ethnicity in Households* (n=3608)**



Sindhi	Balouchi	Muhajir	Punjabi	Pushtoon
25	20	31	12	12

***Figure 9: Division of the population on the basis of language* (n=3608)**



Sindhi	Baluchi	Jadgal	Brohi	Gujrati	Memon	Kathwri	Urdu	Punjabi	Siraiki	Pushto	Hindko	Others
24.3	17.7	0.2	0.8	3.4	15.3	1.7	14.1	9.8	1.1	6.8	4.0	0.9

3.1.1.2 Socio-demographic characteristics

The Socio-demographic characteristics of the Households are given below

Table 7: Socio-demographic characteristics of the Households

Variables	n	%	Mean	Std. Dev.
Gender	**3608**			
Male	1840	50.8		
Female	1768	49.2		
Age distribution				
Male			23.59	17.21
< 25 years	1116	60.3		
≥ 25 years	734	39.7		
Female			24.43	17.10
< 25 years	999	56.8		
≥ 25 years	759	43.2		
Residence in Same Household			**21**	**21**
≤ 10 years	1660	46.0		
11 - 30 years	1226	34.0		
> 30 years	722	20.0		

Variables	n	%	Mean	Std. Dev
Residence in Lyari			**35**	**19.6**
≤ 5 years	325	9		
6 -10 years	289	8		
11 – 15 years	289	8		
16 – 29 years	721	20		
≥ 30 years	1984	55		
No. of person HH			**7.7**	**5.4**
≤ 7	1716	47.56		
8 – 10	984	27.26		
11 – 15	655	18.00		
≥ 16	253	7.01		
Marital Status				
Single	2165	60		
Married	1263	35		
Divorced / Separated / Widowed	180	5		
Education				
Illiterate	1075	29.8		
Madressa / Primary	1263	35.0		
Secondary / Matriculation	928	25.7		
Intermediate / Bachelor / Masters	238	6.7		
Employment Status				
*Student or unable to work	1504	41.7		
Unemployed	660	18.3		
¥Employed	938	26.0		
Housewife	437	12.1		
Did not know	69	1.9		

* it include students/too young, physically handicapped and bed ridden.

¥ includes working on daily wages, self employed and working for monthly wages.

Sixty five percent of the persons were born in lyari while 18% were born in other areas of Karachi. The rest (17%) were born outside Karachi.

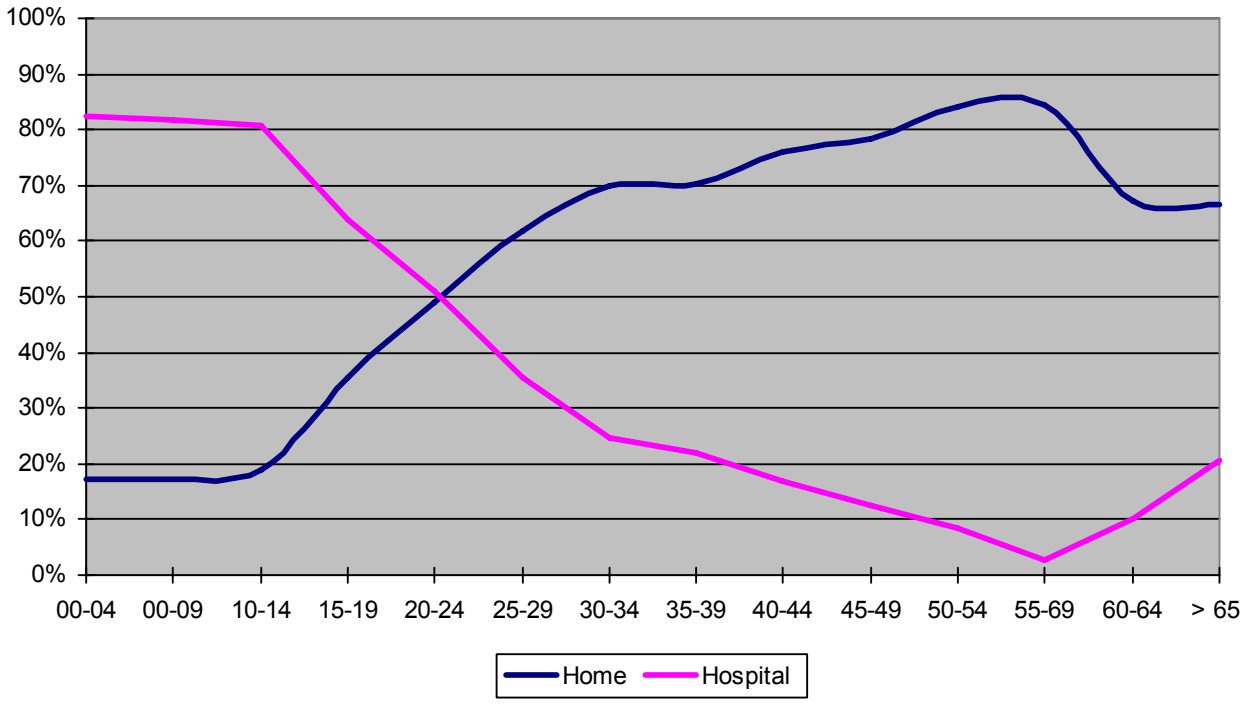


Figure 10: age distribution for place of birth

At five year differences of age we observed that the older the person more the chances of his being born at home.

On the basis of home or hospital delivery we found that 52% of all individuals were born in hospital or maternity home while the rest were born at home.

3.1.1.3 Section A2 gathered information about the household diet with reference to fat, oil and salt intake. In 57% households at least 6 persons eat at home while in 31% at least 10 persons eat at home while in 10% households more than 12 persons eat at home. On an average 7 persons per household eat at home every day.

Table 8: Use of Fat and Salt in Households

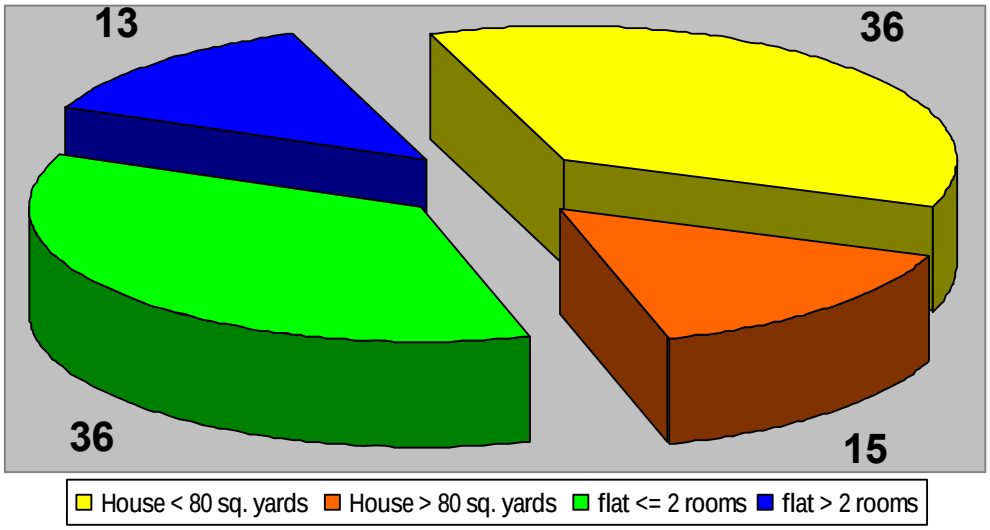
Variable	n = 532	%	Average Consumption per month
Type of fat for cooking			
Banaspati Ghee (Saturated And Trans fatty acids)	**80**	**15.0**	4.0 ± 3.0 Kgs per month
Cooking Oil	**218**	**41.0**	4.9 ± 3.4 Kgs per month
Combined Banaspati Ghee and Oil	**221**	**41.5**	
Other Oils	**13**	**2.5**	

Salt use per month			
< 1000 gm	**211**	**39.7**	
1000 – <1500 gms	**301**	**56.5**	
1500 – <2000 gms	**10**	**1.9**	
≥ 2000 gms	**10**	**1.9**	

3.1.1.4 Section A3 had questions to assess the socioeconomic status.

Although 98% houses had permanent walls only 86% had permanent roof. Around 59% had their own houses while the rest were on rent. The average rent was estimated to be around 1,500 Pakistani rupees per month.

Figure 11: Type of Residence



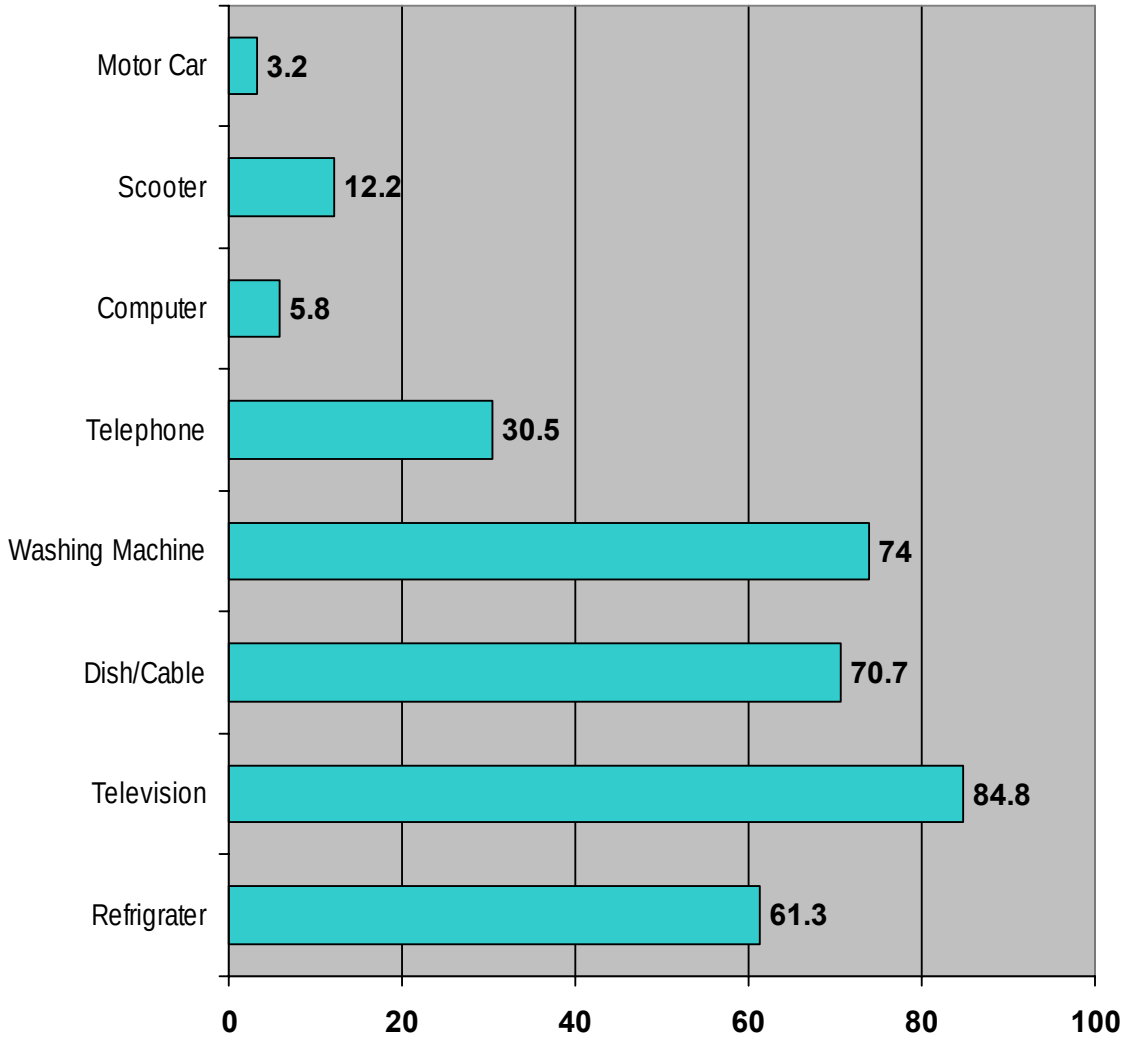
Taking into account the number of rooms in a household 29% were living in a house having > 3 rooms excluding the kitchen and toilets. A separate kitchen was present in 66% of the households while the rest used either part of a room (13%) or the open space (20%) as a kitchen.

As regards the water sanitation condition in each household nearly 90% had bathing water indoors. Of theses bathing facilities 80% was also used for drinking purposes will the remaining 20% houses used other sources of drinking water.

As regards the hygiene and sanitation condition we asked about the type of toilet used to assess waste disposal facility. Around 79% used a flush latrine at home while 1% used a latrine outside the house (80% used a flush latrine). Around 11% used a close pit while 5% used a bucket and 4% used to defecate in the open space.

We also collected data about the household items available in the households visited.

Figure 12: Household Items



Refrigrater	Television	Dish/Cable	Washing Machine	Telephone	Computer	Scooter	Motor Car
61.3	84.8	70.7	74	30.5	5.8	12.2	3.2

Almost all (99.6%) households had electricity while 95.6% had sui gas at home.

Table 9: Monthly and Annual Income

Monthly Income in Pak. Rupees at Household level	n	%	Average Income per month
≤ 3000	156	29.3	
>3000 - <5000	103	19.4	5,000
≥ 5000 - <8000	158	29.7	
≥ 8000 - <10000	24	4.6	
≥ 10000	91	17.0	

The average annual income was calculated to be Pakistani Rupees 54,500.

3.1.1.5 Section A4 showed the morbidity and mortality of each household. This also included the type and cost of treatment as well as the number of deaths during the last 3 years In 33% of the households a person had been sick during the last 15 days. Twenty five percent had one person sick during last 15 days while 5% had 2 persons sick during this period. Three percent households had 3 or more persons sick during the last 15 days.

Table 10: Mode of Treatment

Mode of Treatment				
No treatment	**Govt. Hospital or Dispensary**	**Private Hospital**	**Family Physician**	**Cost / Patient Mean ± SD**
5.9%	8.1%	13.0%	73.0%	878 ± 2078

With regards to the mortality in households, in 10% of the households someone died during the last 3 years. Twenty one percent of all deaths were in children less than one year old.

3.1.2 Part B: Individual Section of Questionnaire

A total of 871 persons were approached out of which 867 persons ≥ 25 years gave their consent to be interviewed for our survey (Response rate 99.5%). Thus of all the persons ≥ 25 years residing in the 532 selected households 867 persons were interviewed by the field teams. Part B consisted of 6 sections which collected information about personal and family history from these individual persons.

3.1.2.1 Section B1 consisted of on personal demographics and personal medical history of each person interviewed. The following table gives a summary of the questions asked

Table 11: Personal Demography of Individuals

Variables	n = 867	%	Mean ± SD
Ever Checked your Blood Pressure?			
Yes	**702**	**81.0**	
No	**165**	**19.0**	
Ever told by Physician you have high blood pressure?			
Yes	**172**	**25.9**	
No	**490**	**74.1**	
Did Physician prescribed any medication for high BP?			
Mean Age			**38.5 ± 14.7**
Yes	**130**	**82.8**	
No	**27**	**17.2**	
Did not reply (not included in %)	**15**		
Ever told by Physician you have a heart disease?			
Yes	**51**	**5.9**	
No	**802**	**94.1**	
What was the Heart diseases?			
Mean Age			**42 ± 15**
Angina Pectoris	**27**	**52.9**	
Heart attack	**19**	**37.2**	
Other	**5**	**9.8**	
Ever told by Physician you have kidney disease?			
Mean Age			**30.9 ± 12**
Yes	**54**	**6.4**	
No	**794**	**93.6**	
Ever told by Physician you have diabetes?			
Mean Age			**48 ± 14**
Yes	**46**	**5.4**	
No	**804**	**94.6**	
How your DM was diagnosed?			
Had symptoms	**30**	**65.0**	
Through screening	**16**	**35.0**	
What medications were prescribed to control your DM?			
Diet only	**4**	**9.5**	
Insulin	**3**	**4.8**	
Tablets	**39**	**85.7**	
Have you ever had an attack of stroke?			
Mean Age			**39 ± 24**
Yes	**21**	**2.5**	
No	**833**	**97.5**	
Ever told by Physician you have Asthma/lung disease?			
Yes	**56**	**8.9**	
No	**568**	**91.1**	

3.1.2.2 Section B2 consisted of questions about family medical history. A total of 856 persons answered this section. Mean age was 40.5 + 14 years.

Table 12: Family Medical History

Variables	N=856	%
Consanguineous Marriage of parents		
Yes	**355**	**44.1**
No	**451**	**55.9**
Immediate family member patient of hypertension?		
Yes	**223**	**37.0**
No	**421**	**69.7**
Don't Know	**40**	**3.3**
Which family member?		
Parents	**182**	**81.8**
Offspring	**1**	**0.3**
Sibling	**40**	**17.9**
Immediate family member patient of heart disease?		
Yes	**115**	**18.8**
No	**488**	**80.0**
Don't Know	**7**	**1.1**
Which family member?		
Parents	**93**	**80.8**
Offspring	**4**	**3.2**
Sibling	**18**	**16.0**
Immediate family member patient of Diabetes Mellitus?		
Yes	**131**	**21.3**
No	**424**	**69.1**
Don't Know	**58**	**9.6**
Which family member?		
Parents	**3**	**2.3**
Offspring	**95**	**72.3**
Sibling	**33**	**25.4**
Immediate family member had an episode of stroke ?		
Yes	**55**	**9.1**
No	**546**	**90.7**
Don't Know	**1**	**0.2**
Which family member?		
Parents	**49**	**89.9**
Offspring	**1**	**1.3**
Sibling	**5**	**8.9**

The most common known cause of death was heart attack in both parents.

Figure 13: Cause of Death

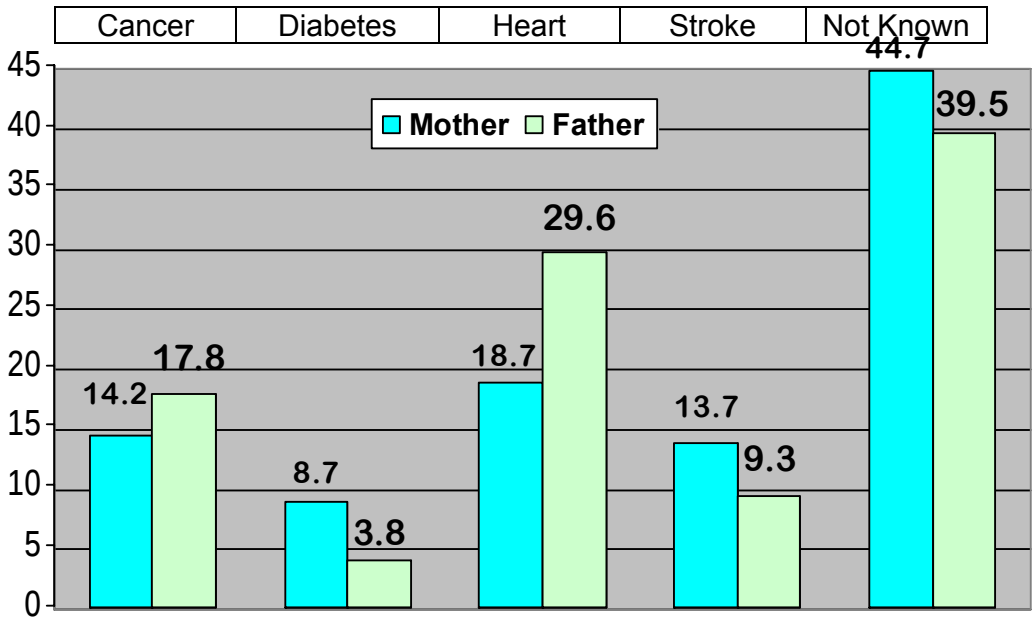


Table 13: Parental Age at Death

Mother	Mean (SD) age at Death	Father	Mean (SD) age at Death
43 %	59.7 (± 19.2) years	63 %	62.5 (± 16.5) years

3.1.2.3 Section B3 contained questions about tobacco consumption and smoking. It was answered by 856 persons. It was interesting to note that the age of first use of these items ranged from 10 to 30 years of age with a mean around 20 years. This section contained details of four different types of tobacco use as given below.

Table 14: Tobacco Consumption

Variable	n	%	mean	Std. Dev.
Ever smoked cigarettes/cigar/beddi?				
Yes	**62**	**10.0**		
No	**555**	**90.0**		
Age when started smoking cigarette/cigar/beddi?			**22**	**11.5**
≤ 18 years	**39**	**63.3**		
> 18 - ≤ 25 years	**10**	**16.5**		
> 25 years	**13**	**20.2**		
Do you currently smoke cigarette/cigar/beddi?				
Yes	**41**	**66.0**		
No	**21**	**34.0**		

Variable	n	%	mean	Std. Dev.
Age when stopped smoking cigarette/cigar/beddi?				
			45	**20**
Are these cigarettes filtered or non-filtered?				
Filtered	**53**	**85.5**		
Non-filtered	**09**	**14.5**		
Average cigarette/cigar/beddi smoked in a day?			**11**	**8**
1 -5	**20**	**32.2**		
6 – 10	**10**	**16.1**		
11 – 15	**03**	**4.8**		
16 – 20	**27**	**43.5**		
> 20	**02**	**03.2**		
Ever smoked huqah/pipe?				
Yes	**53**	**8.6**		
No	**562**	**91.4**		
Age when started smoking huqah/pipe?			**20**	**9.4**
≤ 18 years	**28**	**53.6**		
> 18 - ≤ 25 years	**16**	**29.3**		
> 25 years	**09**	**17.1**		
Do you currently smoke huqah/pipe?				
Yes	**29**	**54.7**		
No	**24**	**45.3**		
Age when stopped smoking huqah/pipe?				
			28.6	**14.5**
Ever use naswar?				
Yes	**38**	**06.2**		
No	**576**	**93.8**		
Age when started using naswar?			**20**	**11.3**
≤ 18 years	**23**	**63.9**		
> 18 - ≤ 25 years	**06**	**16.7**		
> 25 years	**07**	**19.4**		
Do you currently use naswar?				
Yes	**34**	**89.5**		
No	**04**	**10.5**		
Ever chewed pan with tobacco?				
Yes	**126**	**20.4**		
No	**492**	**79.6**		
Age when started chewing pan with tobacco?			**23**	**11.7**
≤ 18 years	**40**	**31.5**		
> 18 - ≤ 25 years	**50**	**39.4**		
> 25 years	**36**	**29.1**		
Do you currently chew pan with tobacco?				
Yes	**110**	**85.3**		
No	**016**	**14.7**		
Age when stopped chewing pan with tobacco?			**32.5**	**14.9**

Average No. of pan with tobacco chewed in a day?			07	08
1 -5	**61**	**50.4**		
6 – 10	**43**	**35.5**		
11 – 15	**08**	**06.6**		
16 – 20	**02**	**01.7**		
> 20	**07**	**05.8**		

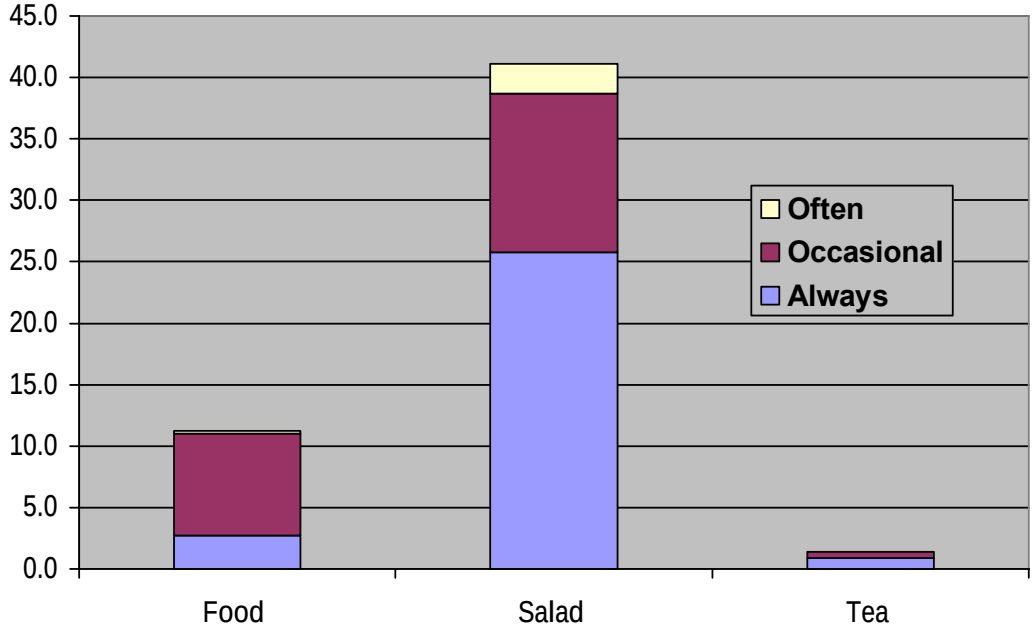
3.1.2.4 Section B4 had 40 questions about personal dietary habits including a list of 33 commonly used food items used on daily, weekly or monthly basis.

Table 15: Food items used on daily, weekly or monthly basis

Items	*% Not using*	Monthly Use (n)	Weekly			Daily	
			n	% use	Days	n	% of use
Eggs	***38.0***	444	338	96.0	4	431	88.0
Parhata	***35.6***	75	60	53.0	1	83	94.0
Nan	***31.1***	118	125	80.0	2	45	82.0
Halwa Puri	***62.9***	88	54	89.0	1	11	100.0
Milk	***71.0***	48	56	57.0	1	72	97.0
Skim Milk	***68.0***	51	78	54.0	1	110	94.0
Cream	***81.2***	53	47	47.0	1	38	100.0
Custurd	***61.0***	254	59	64.0	1	11	64.0
Ice cream	***59.0***	259	69	64.0	1	12	92.0
Yougurt	***29.0***	166	322	52.0	1	113	94.0
Sweet Lasi	***59.0***	165	132	65.0	1	41	95.0
Lassi	***58.0***	161	145	58.6	1	51	94.0
Margirine	***92.7***	21	23	70.0	1	12	100.0
Butter	***80.0***	72	65	58.5	1	28	96.0
Mutton	***56.2***	130	228	52.0	1	12	100.0
Beef	***18.7***	109	561	71.0	2	35	85.7
Chicken	***9.9***	165	600	79.5	2	20	70.0
Fish	***17.7***	235	444	52.0	1	25	80.0
Prawns	***56.0***	211	162	78.4	1	7	85.7
Organ Met	***54.3***	264	114	75.0	1	11	91.0
Junk Food	***60.3***	224	98	56.0	1	21	95.0
Cook Veg	***8.4***	56	651	65.0	2	94	87.0
Cook Potat	***10.0***	58	508	64.0	2	198	95.0
Raw Veg	***30.6***	112	315	76.0	2	159	92.5
Fried Rice	***11.5***	269	464	69.8	1	27	81.5
Legumes	***3.6***	66	689	75.0	2	63	94.0
Fruits	***26.4***	186	252	73.0	2	171	97.0
Fruit Juice	***76.0***	65	97	70.0	1	31	97.0
Bakery Itm	***42.5***	121	190	81.0	2	166	96.0
Desi Sweat	***65.0***	233	42	69.0	1	11	91.0
Fried Items	***36.1***	311	205	80.0	2	26	96.2
Dried Fruit	***76.3***	133	45	91.0	2	15	100.0
Choc tofee	***81.5***	60	30	77.0	2	58	96.6
Others	***72.0***	3	4	100.0	1	31	74.0

Information was also collected about use of additional salt on food, salad and tea from the 867 subjects.

Figure 14: Use of Additional Salt



3.1.2.5 **Section B5** consisted of questions on chest pain on physical exertion. Only 18% reported any sort of chest pain.

Table 16: Chest pain on physical exertion

	n = 867	%
Chest Discomfort		
Yes	**156**	**18.0**
No	**711**	**82.0**
On exertion or climbing stairs		
Yes	**93**	**10.7**
No	**51**	**5.9**
On walking Straight		
Yes	**53**	**6.1**
No	**55**	**6.3**
What do you do when pain occurs?		
Carry on walking	**31**	**3.6**
Slow down and Stop	**67**	**7.7**
Relieved on Standing Still?		
Yes	**39**	**4.5**
No	**26**	**3.0**

Relieved in		
< 10 minutes	**31**	**3.6**
> 10 minutes	**26**	**3.0**
Pain in Left Anterior Chest	**28**	**3.2**
Pain in Left Arm	**2**	**0.2**
Pain in Sternum	**22**	**2.5**
Any other Site	**19**	**2.2**

3.1.2.6 Section B6 had questions about physical activity and exercise during the last 7 days.

This was asked to a total of 867 persons. A majority of the people were not physically active.

Figure 15: Physical Activity

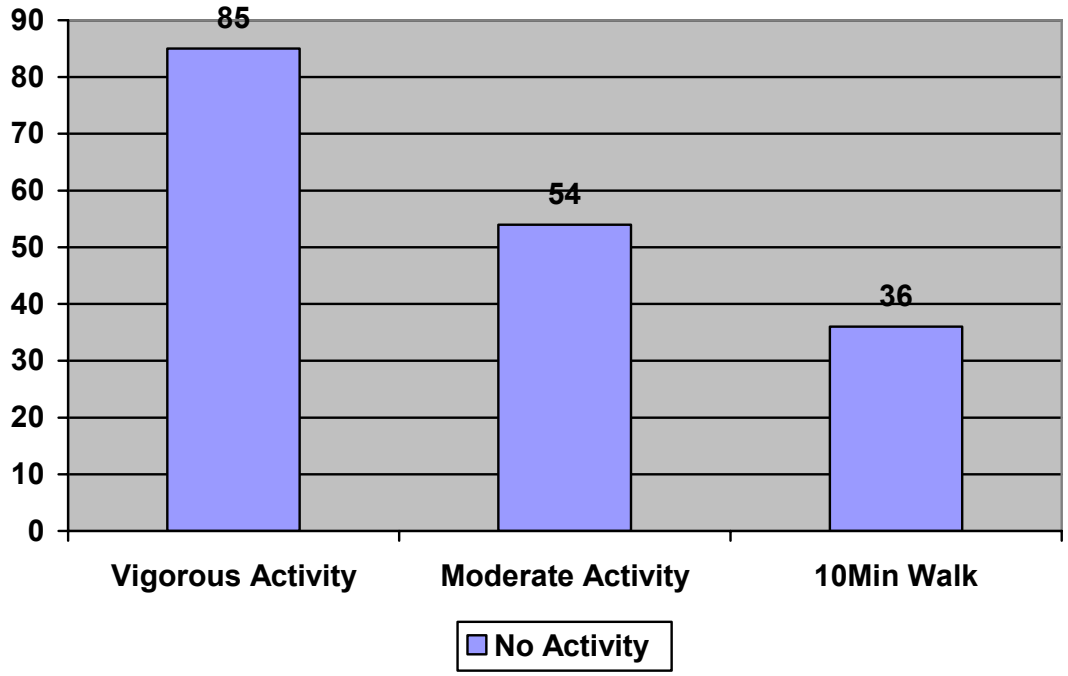


Table 17: Average duration of Physical Activity

Physical Activity	n	Average	n	Average
	Days/ week		Hours / day	
Vigorous Activity	130	4.5 ± 2.5	62	2 ± 1
Moderate Activity	345	5 ± 2.5	254	2.2 ± 1.6
10Min Walk	476	4.4 ± 2.6	333	2.5 ± 1.7
Sitting or Rest	N/A	N/A	607	4.4 ± 2.6

Table 18: Weekly and daily chores of households

	Household Activity	Cooking	House Cleaning	Washing	Running Errands
Number of persons	793	485	422	477	369
Average of 7 days	2.2 ± 6.7	6 ± 1	5.9 ± 2.1	2.6 ± 2.0	4.2 ± 2.5
Number of persons		494	452	483	385
Average of 24 hours		1.8 ± 1.4	4.3 ± 9.7	7.6 ± 1	14 ± 22

3.1.3 Part C: Anthropometry Section of Questionnaire

Anthropometry section included measurements of weight, height, waist and hip circumference. It contained 18 variables. Collected anthropometric data included measurements of weight, height, waist and hip circumference. Participants were asked to wear light clothing and take off their shoes during anthropometry measurements. Height was measured to the nearest cm and weight to the nearest 0.1 Kg. Weight was taken with a standardized scale and height with a standardized measuring stick. Waist circumference was measured as the mid point between the iliac crest and the lower margin of the ribs. Blood pressure was take by a medical student or doctor at least twice with 20 minute intervals, after ensuring that at least 30 minutes had passed since tea or tobacco were last consumed. A third BP measurement was taken if one or both of the first two readings were above the cut-offs for a diagnosis of hypertension.

Table 19: Mean Anthropometry Measurements

	n	Mean
Mid arm Circumference in cms	802	44.2 ± 47.7
Pulse (Beats per minute)		
1st reading	790	80 ± 12.5
2nd reading	734	79.8 ± 13.9
3rd reading	133	75.4 ± 20.3
Systolic Blood Pressure (mmHg)		
1st reading	787	119.7 ± 25.3
2nd reading	743	127.1 ± 50.1
3rd reading	136	126.8 ± 19.1
Diastolic Blood Pressure (mmHg)		
1st reading	787	87 ± 21.4
2nd reading	742	81.5 ± 12.6
3rd reading	138	81.2 ± 14.3

Table 20: Categorical variables of Anthropometry

Variable	n (867)	%	mean	Std. Dev.
Height (cm)			156.9	9.2
Weight (kg)			60.6	15.9
Hip circumference (cm)			95.4	14.0
Waist circumference (cm)			86.1	15.5
BMI				
Under weight (< 18)	**102**	**11.8**		
Normal (18 – 22.9)	**251**	**28.9**		
Over weight (23 - 25)	**112**	**12.9**		
Obese (> 25)	**402**	**46.3**		
Waist Hip Ratio				
Normal (≤ 0.90)	**320**			
High (>0.90)	**547**	**63.1**		
Systolic Blood Pressure			124.	22.6
Diastolic Blood Pressure			81.3	32.3
High Blood Pressure on BP readings				
≤ 130/85 mmHg	**681**			
> 130/85 mmHg	**186**	**21.4**		
New & Previous Case of hypertension	**425**	**49.0**		

At the end of each household visit, all persons who participated in the study were asked to undertake an 8 hour fasting for blood tests (fasting blood glucose, insulin levels and lipid profile) that was collected at home on Saturday and Sunday mornings. They were also provided a urine collection bottle and asked to collect a mid-stream urine specimen for tests (proteinuria and microalbuminuria) on the morning that their blood tests were due.

A total of 867 gave consent to participate in the study. Only 363 persons gave blood samples out of these 867 adults having a response rate of 42% for blood collection.

Table 21: Means of anthropometric and biochemical parameters of subjects

	Male Mean ± SD	Female Mean ± SD	Total Mean ± SD
Age (years)	45.1± 15.7	38.8 ±12.8	40.8 ± 14.1
BMI(kg/m2)	23.9 ± 7.2	26.0 ± 7.1	25.4 ± 7.2
Waist hip ratio	0.94 ± 0.11	0.91 ± 0.16	0.92 ± 0.15
Waist circumference (cm)	89.5 ±16.0	87.8 ± 15.8	88.4 ± 15.8
Systolic Blood Pressure (mmHg)	127.4 ± 18.6	124.3 ± 19.6	125.2 ± 19.3
Diastolic Blood Pressure (mmHg)	84.3 ± 11.8	79.9 ±13.7	81.2 ± 13.3
Fasting Plasma Glucose (mg/dl)	86.7 ± 21.7	86.6 ± 23.2	86.6 ± 22.7
Cholesterol (mg/dl)	175.9 ± 42.6	180.7 ± 44.6	179.2 ± 43.9
Triglycerides (mg/dl)	158.9 ± 105.2	135.2 ± 70.2	142.6 ± 83.3
LDL (mg/dl)	110.7 ± 28.8	116.2 ± 33.0	114.5 ± 31.8
HDL (mg/dl)	37.1 ± 10.4	43.2 ± 12.4	41.3 ± 12.2
Insulin (mU/ml)	7.6 ± 2.7	8.3 ± 4.5	8.0 ± 4.0
Urinary Microalbuminuria (mg/dl)	12.9 ± 12.4	14.9 ± 20.6	14.3 ± 18.3

The biochemical analysis and assessment of risk factors based on these parameters were done on these 363 persons.

Table 22: Cut-off values for biochemical variables

Variable	n (363)	%	mean	Std. Dev.
Cholesterol			**179.3**	**43.9**
≤ 200 mg/dl	**219**	**70.0**		
> 200 mg/dl	**94**	**30.0**		
Triglycerides			**142.6**	**83.3**
≤ 150 mg/dl	**210**	**69.5**		
> 150 mg/dl	**92**	**30.5**		
Low Density Lipoprotein (LDL)			**114.5**	**31.8**
≤ 130 mg/dl	**225**	**71.9**		
>130 mg/dl	**88**	**28.1**		
High Density Lipoprotein (HDL)			**41.3**	**12.1**
≥ 40 & 50 mg/dl	**96**	**30.8**		
< 40 & 50 mg/dl	**216**	**69.2**		

Fasting Blood Glucose			**86.6**	**22.7**
≤ 100 mg/dl	**227**	**85.0**		
> 100 - ≤ 126 mg/dl	**15**	**5.6**		
> 126 mg/dl	**25**	**9.4**		
HOMA - IR			**1.7**	**0.8**
> 25th Percentile	**64**	**25.7**		
< 75th Percentile	**185**	**74.3**		

3.1.4 Prevalence of abnormal glucose tolerance

Prevalence of Diabetes was found to be 9.4% in our study. Of these 2.6% were known cases of diabetes while 6.8 % were new cases of Diabetes. Based on the Fasting criteria of IFG (FPG between 125 – 100 mg/dl) we identified 5.6% cases. Thus a total of 15% were found to have abnormal glucose tolerance.

Figure 16: Prevalence of Diabetes and IFG

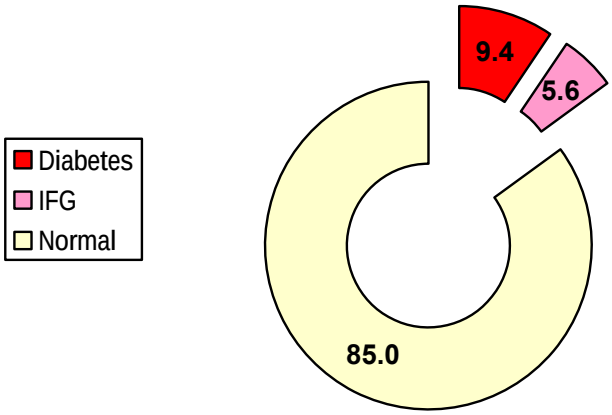
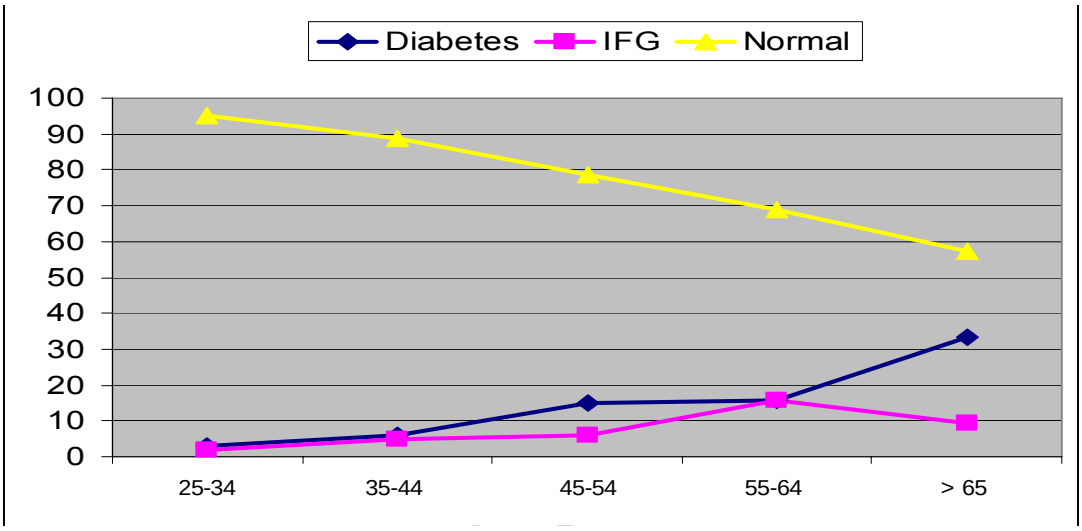
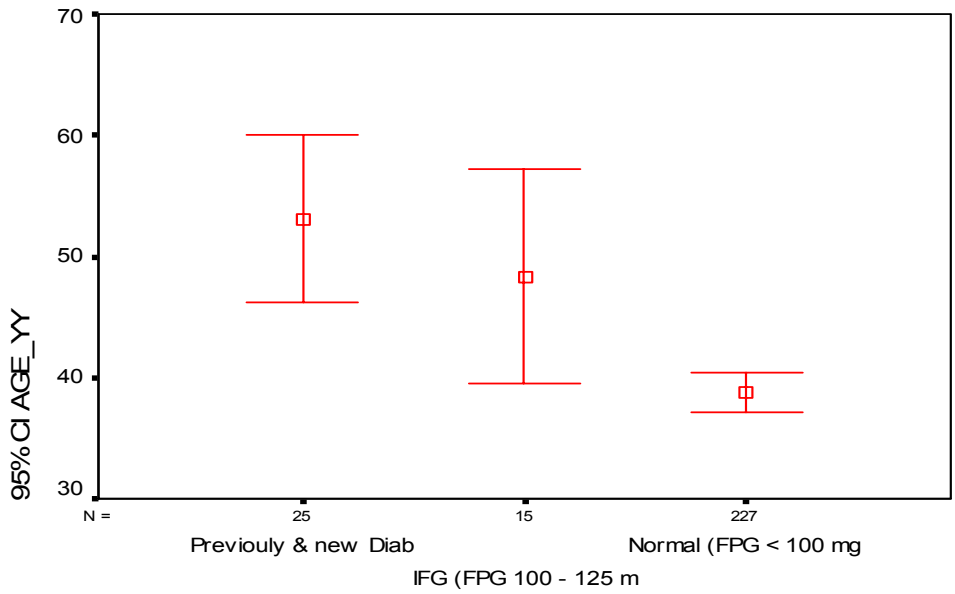


Figure 17: Age Distribution of Prevalence of glucose tolerance



We observed that as age advanced the number of Diabetes and IFG cases also increased. This was also evident by plotting Error Bar which showed that Diabetes and IFG subjects had a higher mean age and range compared to normal subjects.

Figure 18: Error Bar of Glucose Tolerance with Age



3.1.5 Distribution of cardiovascular disease and its risk factors

We identified 20 cases of cardiovascular disease out of 363 persons on the basis of self reporting of CVD showing a prevalence of 5.5%. Risk of CVD was 3 times [OR 3.07; 95% CI (1.08-8.73)] in subjects with hypertension compared to non hypertensive subjects. Those having a waist hip ratio more than 0.90 had 3 times more risk of CVD compared to those with normal WHR [OR 3.08; 95% CI (0.88-10.87)]. Smokers had twice risk of CVD compared to non smokers [OR 1.93; 95% CI (0.70-5.26)]. Diabetics had nearly two times risk of CVD compared to non diabetics [OR 1.79; 95% CI (0.38-8.28)],

Table 23: Risk Factors of CVD

Variable	CVD n =20	Normal n = 342	OR (95% CI)
Age	Mean 49.6 SD (±12.4)	Mean 40.4 SD (±14.1)	4.97 (1.63-15.38)
Hypertension (%)	73.7	47.7	3.07 (1.08-8.73)
High Waist Hip Ratio (%)	78.9	61.1	3.08 (0.88-10.87)
Family History for CAD (%)	13.3	18.8	0.66 (0.14-3.07)
Current Smoker (%)	31.6	19.3	1.93 (0.70-5.26)

Variable	CVD n =20	Normal n = 342	OR (95% CI)
BMI (> 23 kg/m2) (%)	55.6	59.5	0.85 (0.33-2.21)
Diabetes (%)	20.0	8.4	1.79 (0.38-8.28)

3.1.6 Descriptive analysis of persons taking blood tests

Around 363 persons gave blood samples and details of their descriptive analysis are given in table 24.

Table 24: Age and Gender distribution of variables in subjects of blood tests

Age	25 -34	35 - 44	45 -54	55 -64	> 65	Total	p value
Male	n=37	n=30	n=15	n=18	n=17	n=117	
Female	n=107	n=68	n=31	n=28	n=12	n=246	
Overall	(n=144)	(n=98)	(n=46)	(n=46)	(n=29)	(n=363)	
Diabetes (%)							
Male	4.8	0.0	18.2	0.0	30.0	7.5	0.014
Female	2.5	8.9	13.6	26.3	36.4	10.2	0.001
Overall	3.0	6.2	15.2	15.6	33.3	9.4	0.000
IFG (%)							
Male	0.0	0.0	9.1	15.4	25.0	5.0	0.014
Female	2.5	7.1	4.5	15.8	9.1	5.9	0.001
Overall	2.0	4.9	6.1	15.6	9.5	5.6	0.000
HTN (>130/85 mmHg) (%)							
Male	40.5	53.3	60.0	50.0	64.7	60.0	0.480
Female	26.2	54.4	71.0	78.6	75.0	48.0	0.000
Overall	29.9	54.1	67.4	67.4	69.0	49.0	0.000
WHR > 0.90 (%)							
Male	45.9	66.7	69.2	72.2	75.0	62.3	0.160
Female	49.1	70.1	77.4	82.1	75.0	63.5	0.001
Overall	48.3	69.1	75.0	78.3	75.0	63.1	0.000
OW (BMI 23-25 kg/m2) (%)							
Male	8.1	16.7	16.7	35.3	31.3	18.8	0.080
Female	15.0	7.6	6.5	7.1	0.0	10.2	0.066
Overall	13.2	10.4	9.3	17.8	17.9	12.9	0.136
Obese (BMI > 25 kg/m2) (%)							
Male	43.2	40.0	33.3	17.6	12.5	33.0	0.080
Female	39.3	60.6	71.0	67.9	41.7	52.5	0.066
Overall	40.3	54.2	60.5	48.9	25.0	46.3	0.136
Cholesterol > 200 mg/dl (%)							
Male	20.7	37.5	35.7	18.8	21.4	26.8	0.516
Female	19.8	34.5	40.7	53.8	41.7	31.5	0.007
Overall	20.0	35.4	39.0	40.5	30.8	30.0	0.028
Triglycerides > 150 mg/dl (%)							
Male	44.4	39.1	35.7	31.3	28.6	37.2	0.850
Female	13.3	37.7	33.3	46.2	33.3	27.4	0.002
Overall	20.5	38.2	34.1	40.5	30.8	30.5	0.043

LDL > 130 mg/dl (%)							
Male	27.6	20.8	42.9	18.8	21.4	25.8	0.550
Female	19.8	29.1	37.0	53.8	33.3	29.2	0.013
Overall	21.6	26.6	39.0	40.5	26.9	28.1	0.080
HDL < 40 & 50 mg/dl (%)							
Male	69.0	60.9	57.1	62.5	78.6	65.6	0.750
Female	65.6	76.4	66.7	84.6	66.7	70.8	0.309
Overall	66.4	71.8	63.4	76.2	73.1	69.2	0.645
Proteinuria (%)							
Male	3.7	0.0	0.0	0.0	0.0	1.1	0.660
Female	2.5	6.3	0.0	4.3	10.0	3.9	0.561
Overall	2.8	4.1	0.0	2.7	4.5	2.9	0.821
Micral (%)							
Male	3.7	0.0	0.0	0.0	0.0	1.1	0.660
Female	6.3	8.5	4.8	8.7	10.0	7.2	0.964
Overall	5.7	5.5	3.0	5.4	4.5	5.2	0.983
Tobacco Consumption (%)							
Male	32.4	40.0	33.3	38.9	23.5	34.2	0.820
Female	11.2	16.2	9.7	17.9	8.3	13.0	0.730
Overall	16.7	23.5	17.4	26.1	17.2	19.8	0.533
Family History of Heart Disease (%)							
Male	7.7	15.0	44.4	0.0	0.0	13.3	0.030
Female	19.7	33.3	0.0	18.8	0.0	20.4	0.026
Overall	17.6	27.7	14.8	12.0	0.0	18.4	0.081
Physical Activity (%)							
Male	83.3	93.8	57.1	87.5	44.4	76.9	0.037
Female	55.8	54.1	64.7	61.5	50.0	56.8	0.938
Overall	60.9	66.0	62.5	71.4	46.7	62.7	0.614

3.1.7 Prevalence of Metabolic syndrome – Different Definitions

Metabolic syndrome was assessed by five different definitions as shown in Table 25. Age and gender specific prevalence of metabolic syndrome by different definitions was seen in our sample.

Highest prevalence was observed by modified ATP III and lowest prevalence by WHO definition. Age and gender specific prevalence of metabolic syndrome was also calculated in Table25. The prevalence of metabolic syndrome increases with increasing age in both males and females. Significant differences in the prevalence with respect to age groups by all definitions were found in females only (p values <0.05).

Table 25: Age & gender specific prevalence of metabolic syndrome by different definitions

Age group	n	WHO %	EGIR %	AACE %	ATP III %	IDF %
Overall	363	7.4	15.2	16.9	49	34.8
Male						
25 - 34	37	0.0	8.1	16.2	54.1	31.3
35 - 44	30	0.0	13.3	23.3	56.7	21.4
45 - 54	15	20.0	13.3	26.7	53.3	46.7
55 - 64	18	0.0	22.2	22.2	55.6	25.0
> 65	17	11.8	17.6	17.6	58.8	43.8
Total	117	4.3	13.7	20.5	55.6	31.8
***Female**						
25 - 34	107	1.9	15.9	2.8	27.1	14.9
35 - 44	68	7.4	17.6	20.6	51.5	37.3
45 - 54	31	12.9	19.4	22.6	58.1	60.0
55 - 64	28	25.0	10.7	46.4	78.6	71.4
> 65	12	33.3	8.3	25.0	75.0	66.7
Total	246	8.9	15.9	16.3	45.9	36.1

* p value <0.05 for WHO, ATP III, AACE and IDF

Table 26 gives the prevalence of different components among those who classified as having metabolic syndrome according to five different definitions. All of the subjects have increased Waist circumference as defined by EGIR and IDF definitions. The prevalence of high blood pressure was 86.2% by ATP III, 82.1% by IDF, 78.2% by AACE, 50% by WHO and 47.6% by EGIR. Prevalence of high triglycerides levels was 59.7% by ATP III and 41.9% by EGIR. Prevalence of low HDL levels was 93.1% by AACE which is highest and 75.6% by WHO which is lowest. Microalbuminurea was 42.2% by WHO definition.

Table 26: Prevalence of components of the metabolic syndrome

	WHO n(%)	EGIR n(%)	ATP III n(%)	AACE n(%)	IDF n(%)
Waist hip ratio	43(95.6)	-	-	-	-
Waist Circumf.		32(100.0)	63(81.8)		100(100.0)
High BP (mmHg)	16(50.0)	10(47.6)	56(86.2)	68(78.2)	64(82.1)

High FPG (mg/dl)	22(48.9)	2(8.3)	16(26.2)	17(19.1)	27(33.8)
High Trigly. (mg/dl)	21(50.0)	13(41.9)	53(69.7)	79(68.1)	59(60.2)
Low HDL (mg/dl)	31(75.6)	25(80.6)	69(90.8)	108(93.1)	85(86.7)
***HOMA(>2)**	35(81.4)	-	-	-	-
Micral (>20 mg/dl)	14(42.2)	-	-	-	-

*Homeostasis Model Assessment; All p values <0.001

3.1.8 Risk of IFG and CVD according to metabolic syndrome definitions

The following odds ratio were observed when IFG and CVD risk was assessed by using the different Metabolic Syndrome definitions.

Table 27: Risk of IFG

Metabolic Syndrome	IFG (n =15)	Normal (n=227)	OR (95% CI)
WHO	53.3	0.0	33.43 (16.11 – 69.34)
EGIR	53.3	15.9	6.06 (2.06 – 17.77)
AACE	66.7	13.7	12.65 (4.05 – 39.48)
ATP III	73.3	26.4	7.65 (2.35 – 24.95)
IDF	73.3	26.4	7.65 (2.35 – 24.95)

Table 28: Risk of CVD

Metabolic Syndrome	CVD (n =20)	Normal (n=342)	OR (95% CI)
WHO	15.0	3.2	5.32 (1.36 – 20.89)
EGIR	15.0	15.2	0.98 (0.28 – 3.49)
AACE	30.0	16.9	2.11 (0.77 – 5.71)
ATP III	70.0	47.8	2.55 (0.96 – 6.78)
IDF	55.0	33.5	2.42 (0.97 – 6.02)

3.1.9 Insulin Levels

The insulin levels of 320 subjects was available for analysis while 249 persons had fasting insulin and fasting glucose levels both available. HOMA-IR was calculated and means and percentiles of Insulin and HOMA-IR defined.

Table 29: Total Mean Values of Insulin Levels and HOMA-IR

Insulin Levels		HOMA - IR	
N	**Mean ± SD**	**N**	**Mean ± SD**
320	**8.09 ± 4.02**	**249**	**1.65 ±0.85**

Figure 19: Mean Values of HOMA-IR according to Age

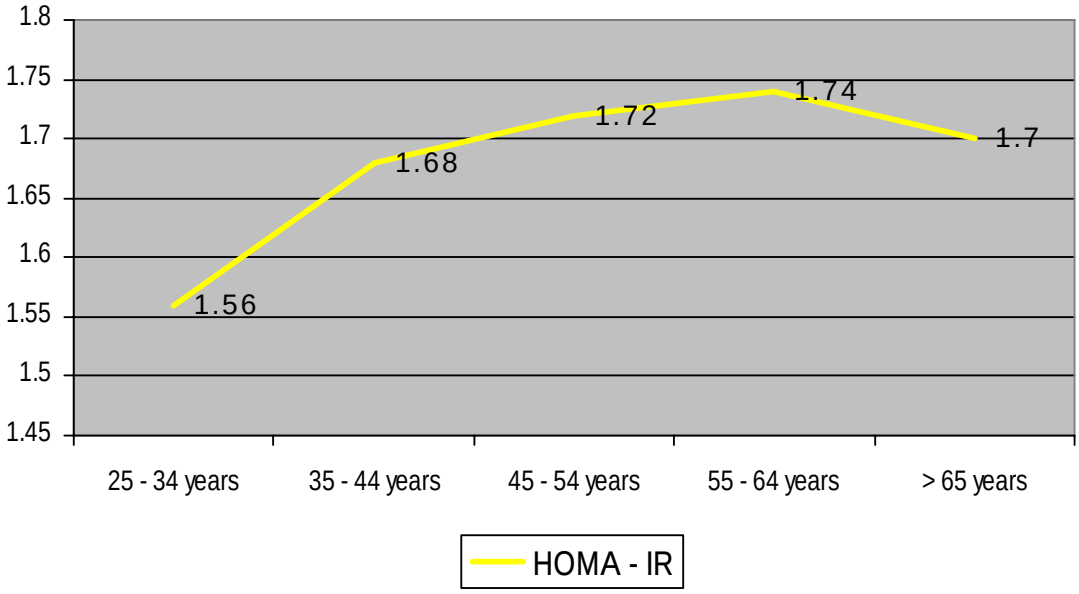
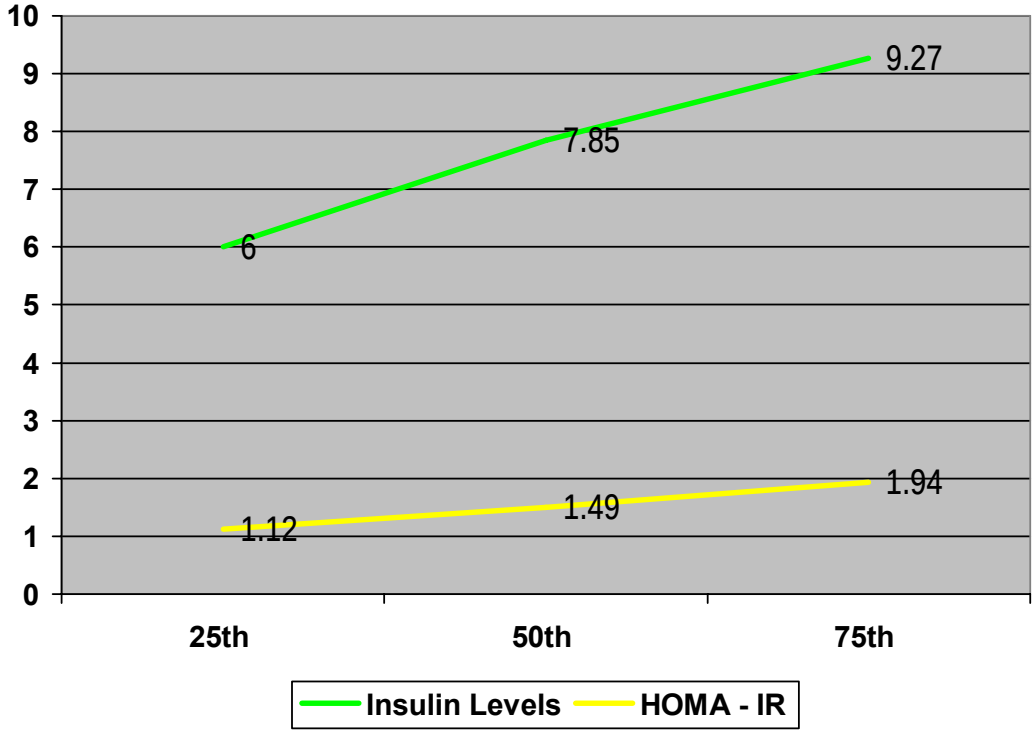


Figure 20: Percentiles of Insulin and HOMA-IR



Chapter 4: Discussion

Discussion

We are in the midst of a twin epidemic of Diabetes and cardiovascular disease which seems to be driven by the metabolic syndrome and the presence of the associated correlates in the metabolic syndrome confers a manifold increase in the risk for T2DM and CVD (56). Thus it is not only a medical, but also a socio-economic need to take all steps to try and prevent the ravages which can be caused by T2DM and CVD (2). The objective of the study was to determine the prevalence of metabolic syndrome in a sample of adults aged 25 years and above from an urban population of Karachi.

4.1 Methodological consideration

4.1.1 Study design

Descriptive studies use routinely collected data which has not been specifically collected for the study during the time of collection of data. A cross-sectional (prevalence) survey is a descriptive study which collects data in a planned way from a defined population at a certain specific period of time. These data are then examined in relation to the presence or absence of the disease under investigation or its severity with a view to test hypothesis and look into associations between various factors.

We planned such a cross-sectional survey in Lyari to establish epidemiological data on metabolic syndrome. Since such type of study is very time and resource intensive, this data is part of a larger collaborative study between Diabetic Association of Pakistan, Baqai Institute of Diabetology and Endocrinology, Interactive research and Development Organisation and a local area NGO – Lyari Community Development Project. The University of Oslo was involved from the start in this study in an advisory capacity. Since I was part of that project as lab field supervisor I have used data from that study.

4.1.2 Selection of Survey Area

Lyari was chosen as it is one of the oldest and densely populated part of Karachi city. Its residents form an extremely diverse community, representing almost every cultural and ethnic group found in Pakistan. There is similarly a wide spectrum of socioeconomic groups present here.

Lyari Town Geographical Information System (LTGIS) was used to define the geopolitical boundaries and population density of Lyari Town. The objective of developing the Lyari Town GIS was to lay the infrastructure for longitudinal follow-up studies of households to assess indicators that may be of interest to researchers, including determining the community-based prevalence of chronic diseases among adults as was done by our group.

4.1.3 Sampling technique

It is usually unnecessary to study the whole population in order to obtain useful and valid information about that population. The investigation of a smaller sample has some advantages such as reduced number of subjects who have to be interviewed, examined or investigated. It provides highly detailed information on smaller numbers. If a sample is used, it is essential to ensure that the subjects included in the sample are representative of the population being investigated. To ensure the representative ness commonly used technique is simple random sampling.
In this sampling technique each subject in the parent population has an equal chance of being selected. One way of obtaining a random sample is to give each subject a number and than to use a computer generated table of random numbers to decide which subjects should be included. This is the method we used to select the 500 households for our study by LTGIS.

4.1.4 Sample size

We assumed that the lower limit prevalence of T2DM to be 11% in this population. The size of the population from which the study sample was to be selected (persons 25 years and older in Lyari Town) was 244,000, the worst acceptable result would be ±1.5% from the true population value. Thus our study would require a sample of at least 713 individuals to have 80% power to detect the true population value.
In the field we were able to interview more than the required sample size (n = 867) but people's reluctance to have the blood tests left us with less than the desired sample size (n = 363) at the end of the study which gave us 40 – 45% power to predict true population value. However since the prevalence of metabolic syndrome is higher (between 20 -25%) compared with diabetes in south Asian population the sample size enabled us to analysis and interpret the results.

4.1.5 Response of the participants and data collection

We depended on the information provided to us by the participants. In our survey the information about personal medical history and family history of disease was dependent on participant's reply as no record of previous medical history or data on socioeconomic status or diet and activity record etc. is available for verification of the answer made by them. Hence we chose to interview the participants and rely on the information given by them.

4.2 Methodological discussion

A number of problems may arise in the design related to cross-sectional surveys and other studies which may invalidate the results unless they are handled properly. Even though this methodology was examined to focus on objectives, some questions on its strength and limitation can be raised.

4.2.1 Strength of the study

Lyari Town Geographical Information System was made to define the geopolitical boundaries and population density of Lyari Town. This was done by dynamically linking the national census database to a purpose built geographical information system (GIS). A year-long, detailed physical survey of Lyari Town was undertaken using available plot maps, most of which were over 20 years old. Although these plot maps required extensive and careful updating, the final results of the physical survey were impressive; all household structures were given a unique identification number, along with all health, education and other civic facilities available to its residents. The edited plot maps were then newly traced, with the unique number ascribed to each household clearly visible and commercial and civic service clearly high-lighted. The new maps were finally digitized using a geo-referenced satellite image of Lyari town at 1 meter resolution. We have already generated a computerized random sample of 500 households from among the 85,520 households households in Lyari Town. There were 11 union councils or subdivisions of Lyari Town where the samples were taken from ensuring that each union council had equal opportunity to be represented in the sample selection.

We expected approximately 1000 adult men and women 25 years and above in the 500 households in Lyari. If members of a household that had been selected refused to consent to household interviews, we knocked on the third door to the right of that house (while standing facing the door of the original house) and seeked consent there. If we were refused again, we knocked on the next consecutive door to the right and repeated this process until we had enrolled a household from the neighbourhood. Individual members within households also reserve the right to refuse participation in the study. Assuming a 10% refusal rate (by members within the household at the time of interview) and another 10% refusal rate by those who decline to provide consent for a blood test, we expected at least 810 individuals to participate in this study.

4.2.2 Limitations of the study

4.2.2.1 Selection Bias

Lyari was chosen as it is one of the oldest and most densely populated part of Karachi city. The rationale of choosing this area was that Its residents form a diverse community representing every major ethnic group found in Pakistan. There is similarly a wide spectrum of socioeconomic groups in the area which could possibly be representative of the general population. However this may not be enough to be representative for the whole of Pakistani population.

By using computerized random selection of households by GIS we hope to minimize the selection bias. As the survey was done on weekdays it included a disproportionate greater number of females compared to males as the men went to work on weekdays and even some on weekends too.

4.2.2.2 Recall and reporting Bias

Subjective data collection in a survey by interview may pose some biases from recall problems. In the answer regarding positive family history of disease we encountered some unknown answers in the participants. Similarly such a problem came during reporting of dietary recall.

Reporting bias can also arise from the standpoint of local cultural context. For example when the field team inquired about household income they noticed underreporting of income.

4.2.2.3 Response Bias

Although 867 adults consented and were interviewed in our survey; only 363 individuals gave blood samples in our study. Response rate was 42%. There could be a response bias in our study with subjects with a particular trend coming more for the blood test causing a selection bias also. To assess this we compared the two groups for compatibility and found that there were 27% males in the 867 sample compared to 32% in the 363 sample. The age, BMI, WHR, and systolic (SBP) and diastolic (DBP) blood pressure was also considerably similar in both the groups (Age = 40.7 vs. 40.8 years, BMI = 24.7 vs. 25.4 Kg/m2, WHR = 0.91 vs. 0.92 cm, SBP = 125 vs. 125 mmHg and DBP= 81 vs. 81 mmHg in the 867 vs. 363 sample).
Since most of the survey form was in as a structured interview questionnaire and subject to response by participants, if a question was not answered a variable would be missing in the final analysis. As regards the anthropometry measurements a 2 day certification course was arranged for the field team for measuring height, weight and blood pressure at the National Institute of Cardiovascular Diseases. Therefore all data was recorded by certified personnel.

4.2.2.4 External validity for generalization

In terms of generalization or external validity the findings of this study reflected the scenario of urban Population. Lyari was chosen as it is the oldest and most densely populated part of Karachi city. Its residents form a diverse community representing every ethnic group found in Pakistan. The sex ratio is similar as for the country (male/female ratio of 1.034 males for lyari vs.1.045 males for the country). The mean age for males in lyari was 23.5 vs. 20.7 years for the country while for females it was 24.5 in lyari vs. 21 years for the country; suggesting similar age and gender distribution as mentioned above for both populations. There is also similarity in the socioeconomic status in lyari and the country with 29% earning less than Pak Rs.3000 in lyari vs. 24% of the population living below the poverty line as defined earlier. Given this we believe that the findings of the study should have a fair representation for the general population. However the sample is too small to be statistically representative for the Pakistani population as a whole and thus the results should be interpretated with caution.

4.2.2.5 Reliability

Blood pressure was taken by a medical student or doctor at least twice with 20 minute intervals to ensure the reliability of the measurements. A third BP measurement was taken if one or both of the first two readings were above the cutoffs for a diagnosis of hypertension.

4.3 Discussion on the findings of the study

4.3.1 Socio-demography of the Sample

The life expectancy is 62.7 years for males and 64.8 years for females in the country while we see in table 13 that the mean age at death of father (males) was 62.5 years while for mothers (females) is 59.7 years for lyari. This and other similarities as mentioned in external validity for generalization may suggest that this could be used as a representative sample for Pakistan.

4.3.2 Prevalence of Abnormal Glucose Tolerance

Prevalence of Diabetes was found to be 9.4%, with overall abnormal glucose control of 15% in our study. The national survey conducted by the Diabetic Association of Pakistan (DAP) in collaboration with the World Health Organization (WHO) during the 1990s reported 11% prevalence of T2DM, with overall abnormal glucose control of 22% (99–101). Conducted in urban and rural areas in the four provinces (NWFP, Balochistan, Punjab and Sindh), the national survey used WHO guidelines for the diagnosis of T2DM and impaired glucose tolerance (IGT) in over 5,600 persons 25 years and above while we used only the fasting criteria. Probably doing OGTT might have yielded a higher prevalence of abnormal glucose tolerance with more cases of IGT compared to 5.6% of IFG. A relative higher prevalence of diabetes was observed in the 45–54 years age groups compared to IFG while the mean age was highest in diabetes followed by IFG and than normal population as shown in figure 17 and 18. Nearly 72% of the subjects did not know they had diabetes while nearly half of the subjects did not know in national survey (99-101).

4.3.3 Risk factors for cardiovascular disease

Although 18% reported chest discomfort in our study the prevalence of CVD was assessed to be 5.5% on the basis of self reporting of CVD. Two hospital based studies in Lahore and Sheikhupura concluded that the prevalence of symptomatic IHD was about 4% and 6% respectively (102).

4.3.4 Prevalence of Metabolic syndrome – Different Definitions

Our data showed that the prevalence of metabolic syndrome ranged from 7.4 – 49% according to the different definitions used. The EGIR and AACE definitions did not include diabetes while ATP III, WHO and modified IDF definitions included diabetes and IGT. The EGIR suggested fasting hyperinsulinemia (upper 25th percentile) as the necessary component of metabolic syndrome. Since WHO and EGIR had a two stage screening process for subjects; fewer individuals qualified for the metabolic syndrome by these definitions.

The prevalence of Metabolic Syndrome according to WHO criteria was low as compared to the other definitions, probably due to the mandatory inclusion of abnormal glucose tolerance cases. Probably due to this few persons qualified for the metabolic syndrome. High percentages of individuals were classified as having Metabolic Syndrome by modified ATP III and IDF criteria for Asians. The prevalence of metabolic syndrome also increases with advancing age. These findings are consistent with other studies [108-113].

When stratified with respect to gender the prevalence was twice in females compared to males by WHO definition (4.3% for males; 8.9% for females). It was slightly higher in females by EGIR definition (13.7% for males and 15.9% for females) and by IDF definition (31.8% for males and 36.1% for females). It was higher in males by AACE definition (20.5% for males; 16.3% for females) and also by modified ATP III (55.6% for males; 45.9% for females).

In Asians, the risk of diabetes and cardiovascular diseases occurs at lower levels of BMI, waist hip ratio and waist circumference compared to Caucasians. Taking this in consideration new cutoff values for Asian Indians have been defined [13,113]. Using these cutoffs for waist circumference and waist hip ratio the prevalence by ATP III was found to be 49% in our study. These observations using the modified ATP III were similar to findings from other studies done in the region showing prevalence ranging from 35.2% to 41% [113 - 114].

The IDF definition also takes into consideration the new cut offs for Asians. The IDF definition assigned different cutoff of central obesity as defined by waist circumference for various ethnic groups to allow better comparison. A lower threshold for fasting plasma glucose in order to detect IGT was also suggested for modified ATP III and IDF.

Compared to our study which showed a prevalence of 34.8% of the metabolic syndrome, the prevalence was 26% according to the IDF definition in the Chennai Urban Rural Epidemiology Study done in India (115). This study showed a prevalence of 49% and 7.4% of the metabolic syndrome in an urban Pakistani population according to the modified ATP III and WHO definition. While other hospital based studies have showed a prevalence of 44% and 46% of the metabolic using ATP III and WHO (diabetic subjects only) definition respectively; this is the first community based study to show the prevalence of metabolic syndrome in our local population (104, 105).

Our investigation was a preliminary study to investigate and explore different definitions of metabolic syndrome in our adult population who along with the other Asian ethnic groups, have different anthropometric characteristics in comparison with Caucasians. Metabolic abnormalities are present at a lower waist circumference in South Asians compared to Caucasians suggesting that modified ATP III criteria might be better at estimating the prevalence of metabolic syndrome in South Asians.

Although the prevalence of metabolic syndrome by using modified ATP III definition was higher than IDF definition (49% vs. 34.8%) the risk for IFG cases was significantly higher in IDF definition compared to ATP III (OR 7.65 vs. 2.25). The risk for CVD was almost the same by both the definitions (OR 2.42 vs. 2,55).

Based on the observations of the present study and those from other investigators, it is suggested that inclusion of modified waist circumference and BMI cutoffs as done in the modified ATP III and IDF definition would probably help metabolic syndrome prediction of diabetes and CVD more precisely.

The modified ATP III and IDF definition aims to address both clinical and research needs and represents a step towards facilitating international consensus.

4.3.5 Prevalence of Components of the metabolic syndrome

Each risk factor of metabolic syndrome has its own variability based on its regulation through both genetic and acquired factors. The different prevalence rates of the various components of the metabolic syndrome were probably due to the variability in the cutoff values used by the different definitions.

The study also shows that there is greater prevalence of hypertension, obesity and low HDL in metabolic syndrome group by any definition. Thus the contributing causes of this syndrome are similar everywhere. There appears to be a very high prevalence

of low HDL cholesterol in our metabolic syndrome group ranging from 75.6% to 93.1%. A similarly high prevalence of low HDL cholesterol in women was seen in an Indian study (111).

4.3.5.1 Hypertension:

Our study found that 49% of the subjects were hypertensive in the community. Out of these 27.6% were known hypertensives while 21.4% were newly diagnosed on the basis of blood pressure readings as shown in table 20.

Another study done in Karachi found that more than 50% of the subjects were hypertensive but this was done in type 2 diabetic subjects (116).

4.3.5.2 Obesity:

Since there is increased cardiovascular risk among Asian people at a lower waist circumference compared to European populations, the World Health Organization (WHO) and the International Diabetes Federation (IDF) have adopted the definition of overweight and obesity in Asians as a BMI of 23 kg/m2 or above and 25 kg/m2 or above respectively, while central obesity was defined as a waist circumference of 90 cm or above in men and 80 cm or above in women (117).

In our study it was observed that 68% of women and 46% of men were obese according to the Asian cut off criteria for waist circumference. Similarly using BMI criteria for Asians in another study done in Hub we found 18% to be obese while 27% were found to be overweight (118). Analyzing the data of 8972 individuals of the National Health Survey of Pakistan it was found that a quarter of the population would be classified as overweight or obese on the basis of Indo-Asian-specific BMI cutoff values (119).Thus it seems that the obesity epidemic is affecting not only the affluent nations but the developing countries are also facing a similar threat and Pakistan also seems to be one of them.

4.3.5.3 Dyslipidemia:

Our study revealed that 30.5% of the people in the community were having high(>150mg/dl) triglyceride levels and 69.2% people were having low (< 40mg/dl for males and <50mg/dl for females) HDL levels. The characteristic lipid disorders seen in this syndrome are high triglycerides and low levels of HDL-cholesterol often with normal levels of LDL- cholesterol (120).

Studying the association between biochemical parameters and obesity indicators in Pakistani children it was observed that those children who were in the uppermost

tertile of arm fat % had significantly higher total cholesterol, triglyceride and LDL-C levels (121). Thus the need to implement programmes to stop our children from becoming overweight so that they do not develop metabolic syndrome in the future.

4.3.6 Defining Insulin Resistance according to Homa-IR

4.3.6.1 Homeostasis model assessment (HOMA)

HOMA was developed by Matthews as a method for estimating insulin sensitivity from fasting serum insulin and fasting plasma glucose (122). The non-linearity of the model precludes an exact algebraic solution, but estimations are possible by using mathematical approximations:

HOMA-B = Insulin (mU/ml) × 20/ glucose (mmol/l) - 3.5

HOMA-R = Insulin (mU/ml) × glucose (mmol/l)/22.5

The model has been incorporated into a simple MS-DOS-based computer program that allows rapid and more accurate determinations of HOMA-B and HOMA-R (123). Low HOMA values indicate high insulin sensitivity, whereas high HOMA values indicate low insulin sensitivity.

Matthews found HOMA ranges between 1.21 and 1.45 in normal subjects in his study while the mean values was between 1.12 to 1.94 in our subjects (122).

The 75th percentile of HOMA-IR was used as a cut-off for insulin resistance and it was found to be HOMA-IR =1.94.

A large number of epidemiological and clinical studies have firmly established consistent correlations between certain anthropometric and metabolic variables of insulin resistance. These variables include obesity, unfavourable body fat distribution, glucose intolerance or type2 diabetes, hyper-insulinemia, low levels of HDL , hyper-triglyceridemia, high levels of LDL and hypertension (124). In our study it was seen that Homa – IR increases with age and some of the variables mentioned above may be affected by this association of insulin resistance with age as obesity, risk of diabetes and hypertension as well as dyslipidemia all increase with age.

Chapter 5. Conclusions, Recommendations and Future Research Implication

5.1 Conclusions

In summary we conclude that the prevalence of the metabolic syndrome was found to be between 7.4% - 49% using the various definitions of metabolic syndrome.
Using different definitions, prevalence of the metabolic syndrome has been reported consistently to range from 10% to 40% in most Asian countries..

We focused on the ATP III and IDF definitions as they provides a diagnostic tool which is suitable for use in populations around the world and established a list of potential additional criteria that could be included in epidemiological studies and other research into the metabolic syndrome.

The prevalence of metabolic syndrome increases with advancing age for both males and females. More than half of our study population does not do any sort of physical exercise and lead a sedentary lifestyle. Thus we find that the contributing causes of this syndrome are similar everywhere with obesity and sedentary lifestyle in the forerun.

Unless preventive programs are properly designed and implemented, we will continue to treat the majority of the cases when they have reached the steeper extreme of the road; when many have already developed the complications of the metabolic syndrome in the form of diabetes and cardiovascular diseases.

Based on the findings of this study we made the following recommendations

5.2 Recommendations

1. The primary management goals of the metabolic syndrome are to reduce the risks of diabetes and cardiovascular diseases. The metabolic syndrome should be considered as a prime target for preventive medicine; as the emerging global epidemic of metabolic and vascular disease has significant implications for the development of population based health policies.

2. Despite the challenges involved in day-to-day life, the non-pharmacological lifestyle modification approach to prevention of the metabolic syndrome is highly effective. This was observed in the Finnish Prevention Trial where none of the people who achieved at least four of the intervention goals developed diabetes during the observation period of 10 years.

3. Need for a diabetes prevention and control program is particularly relevant in Pakistan as increased inherent predisposition, younger age of onset, lack of capacity to effectively treat the condition at the primary healthcare level and lack of access to healthcare system for possible complications makes a strong case for investment in diabetes prevention and control programmes.

4. A large number of lifestyle-related risk factors are associated with the metabolic syndrome and diabetes. These include family history, smoking, physical inactivity, watching television, consuming fast foods and high-sugar drinks and low socio-economic status. To increase people's awareness seminars and public events should be arranged to highlight the significant of a healthy lifestyle.

5. WHO and IDF has made recommendations to governments worldwide for the development of nationwide surveillance and prevention programmes against non-communicable diseases, including diabetes. However, the combined efforts of communities, governments and advocacy groups are needed to translate this evidence into clinical practice.

5.3 Further research implication

1. Metabolic Syndrome definitions have to be assessed for predicting future cases of IGT/IFG and diabetes in Asian populations. Thus a prospective study of 3 years duration needs to be initiated to follow subjects with and without the metabolic syndrome to observe how many become IGT/IFG or develop diabetes after 3 years. This will help to monitor disease trends and a further 2 year follow up to observe how many of the IGT cases identified during this period progressed to diabetes with give a better understanding of the predictive value of the metabolic syndrome.

2. In several randomized trials, drug intervention has shown to be less effective than therapeutic lifestyle interventions in the prevention of type 2 diabetes. We need to evaluate the efficacy of lifestyle modifications and drugs as a means of primary prevention in a population with similar environmental conditions and genetic propensity as the Pakistani population such as the recent Indian Diabetes Prevention Programme.

3. Policy changes and community mobilization schemes need to be initiated. Lifestyle modification programmes with emphasis on increasing physical activity (30 minutes of brisk walking), adhering to a balanced diet (high in fibre and low in fat), and losing body weight has shown to reduce the risk of progression from impaired glucose tolerance to diabetes in up to 58% cases.

4. The involvement of a multidisciplinary team to reach targets and improve adherence to treatment has also been shown to reduce death and disability by up to 70% in people with established diabetes.

5. These programmes will aim to collect population based data, monitor disease trends and create an environment that will help in promoting healthy lifestyles through multi-sectoral and inter-disciplinary collaborations.

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Appendices

Informed Consent

Diabetic Association of Pakistan and World Health Organization Collaborating Center

CONSENT FORM

Title of Research Project:

Prevalence of Type 2 Diabetes and Associated Risk Factors among Adults 25 Years and Above in Urban Karachi

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Explanation of Research Project:

PURPOSE OF STUDY

The doctors and health workers here are working with researchers at

1. Diabetic Association of Pakistan and World Health Organization Collaborating Centre;
2. Interactive Communications Research and Development Division;
3. Baqai Institute of Diabetology and Endocrinology
4. Lyari Community Development Project

to find out about diabetes and heart disease in adults. Your household has been selected randomly from a list of all households in Lyari / North Nazimabad. The researchers undertaking this survey would like to ask you to participate in this study.

PROCEDURES

If you agree we will ask you questions about

1. your household and members of your household.
2. your lifestyle (e.g. diet, exercise) and existing conditions related to diabetes and heart disease.

We will take measurements of your height, weight, hips, waist, abdomen and blood pressure. The doctors would like to take a blood sample from you after you have fasted overnight to test for high levels of glucose, lipids and liver enzymes. You will be informed of the glucose test results within 3 days but the results of some of the other tests will take longer.

Do you agree to provide blood to test for glucose, lipids and liver enzymes: Yes __; No ___

We would also like to store your blood sample to test for infections that might cause liver disease. The blood sample may be stored for up to 10 years. The samples will be stored in a manner that will not identify you by name. The results from these future tests may not be available to you.

Do you agree to let the blood sample be stored for up to 10 years for future research? Yes ____; No _____

The data from the study will be kept in an office in Karachi. Information about your child will be available only to people working on the study. We will keep the study information private to the extent possible by the laws of Pakistan. People responsible for making sure that the research is done properly may review your study records. This might include people from the

Baqai Institute of Diabetology and Endocrinology and the Lyari Community Development Project.

RISKS AND DISCOMFORTS

If blood is taken the needle stick may cause some discomfort and bruising.

BENEFITS

The test results will be given to you. Any doctors that you visit will benefit by finding out if you have diabetes or risk factors for diabetes and heart disease. This information will also help researchers and doctors in understanding the causes of diabetes and heart disease in adults in Lyari / North Nazimabad and to plan programs to prevent these diseases. If you do not have diabetes or risk factors for diabetes and heart disease, you will be able to continue your lifestyle knowing that you are at low risk. You will not receive any payment for participating in this study.

You are not forced to be in this study. You may leave the study at any time. If you decide not to be in the study, your care or relations with your doctors will not be changed in any way. You should ask the project coordinator any questions you may have about this study. You may ask him/her questions in the future if you do not understand anything. The researchers will tell you any new information that they may find out while you are in this study.

If you think being in the study has hurt you, you have not been treated fairly you can call the Principal Investigator Dr. A Samad Shera at 661-6890 (Karachi). You can also call the Project Coordinator Dr. Aamir Khan at 439-6254 (Karachi). You can also call Dr. Abdul Basit at the Baqai Institute of Diabetology and Endocrinology at 661-7234 (Karachi) and Mr. Abdur Rahim Moosvi at the Lyari Community Development Project at 752-1687 (Karachi).

If you agree to participate in this study please sing your name below.

_____
Signature

_____
*Witness to Consent Procedures**

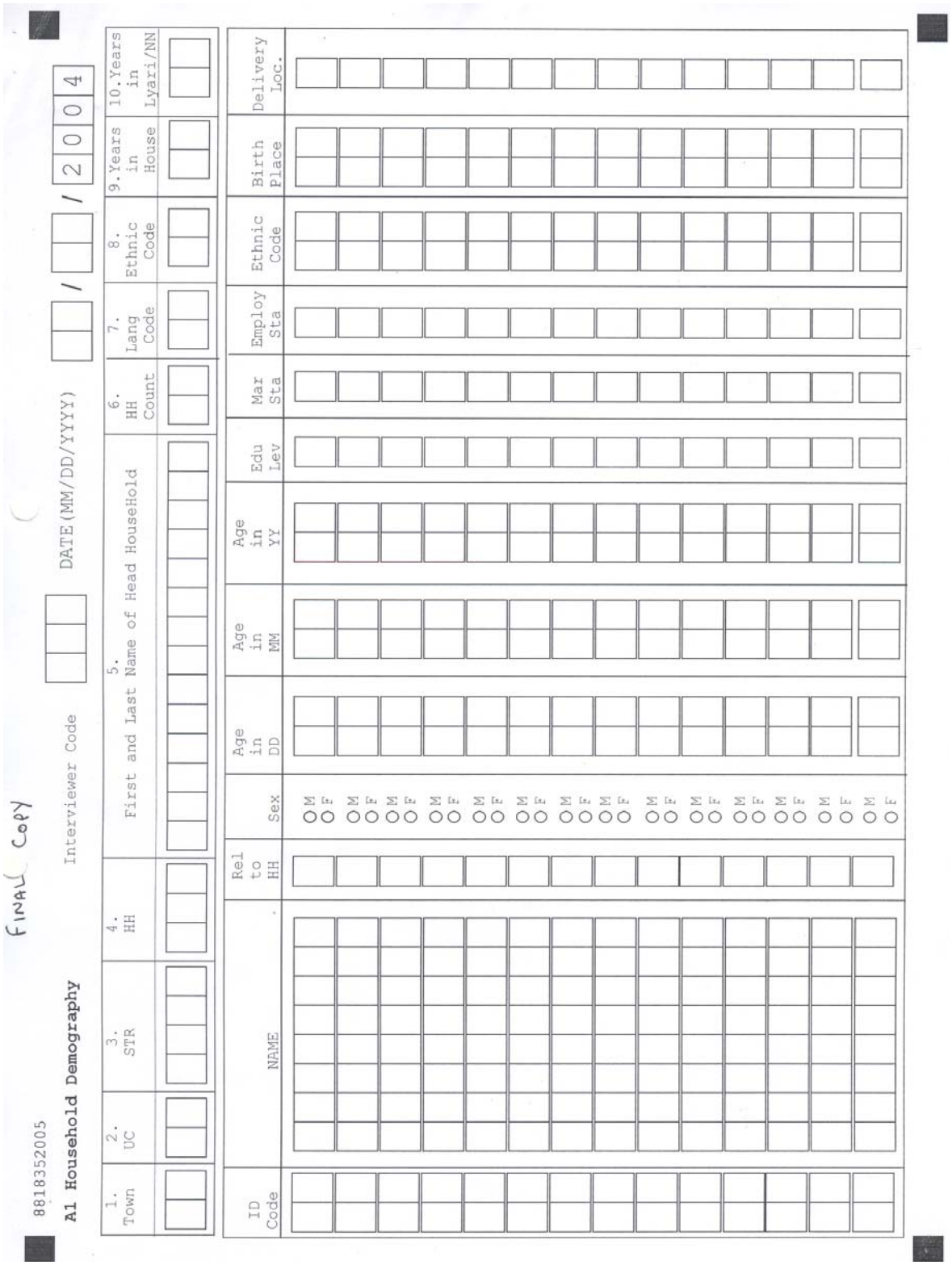
_____
Signature of Investigator

_____
Date
**Optional unless subject is illiterate, or unable to sign*

Void One Year From Above Date
No. _____
Approved From _____ to _____

Note: *Signed copies of this form must be a) retained in file by the Principal Investigator, b) given to the participant and c) put in the patient's medical record (when applicable).*

Structured Interview Questionnaire (11 Pages)



6705376734 IC House UID

A2 House Hold Diet

A2.1 What kinds of fat do you usually use in cooking (e.g. cooking salan, frying etc.)?	☐ Banaspati Ghee ☐ Asli Ghee ☐ Oil ☐ Butter ☐ Margarine
	Others
A2.2 What brand of Ghee/Oil do you use?	Ghee Oil
A2.3 How much banaspati ghee do you use per day or per week? No Frequency 1 Daily 2 Weekly 3 Monthly	KG GM
A2.4 How much Asli ghee do you use per day or per week No Frequency 1 Daily 2 Weekly 3 Monthly	KG GM
A2.5 How much oil do you use per day or per week? No Frequency 1 Daily 2 Weekly 3 Monthly	KG GM
A2.6 On an average how much salt do you buy (packets) in one month?	Pack gm/pack
A2.7 Do you usually use same food dishes in lunch and dinner?	○ Y ○ N
A2.8 For how many people, above age 1, is food cooked at home daily?	

7991431464 IC House UID

A3 Socioeconomic Status

A3.1	Main Type of construction of house Roof Walls Floor	1.Pucca 2.Semi-pucca 3.Katcha — R W F
A3.1a	What is the house type/size	1.Hut 2.House(<80 sq.yards) 3.Town House (80-240 sq.yards) 4.Bunglow (300-500 sq.yards) 5.Bunglow (500+ ssq.yards) 6.Ordinary Flat(2 rooms or les) 7.Luxury Flat(3 or more rooms)
A3.2	Do you own this house	1.Yes,Own, 2.No,on rent 3.No,office accommodation 4.No,relative house
A3.2a	What is the monthly rent or expected rent, if owned?	Amount in Rs 99999. Dont know
A3.3	How many rooms are altogether in this house(excluding Kitchen,bath/toilet, store,veranda)?	write actual number of rooms •if more than one households in one structure,ask how many of these are used by this household
A3.4	What is the main source of water this house hold uses for bathing and washing.	1.Tap inside 2.Hand Pump Inside 3.Well/boring inside 4.Community Tap; 5.Community Hand Pump ;6.Community well/boring 7.Tanker; 8.Other.please specify; 9.Water Bought — if others pls specify / Others
A3.4.1	Does this household get drinking water from the same source?	1.Yes,same source 2.No,bottled water 3.No,other tap; 4.No, other hand pump; 5.No,other well/boring; 6.other..please specify — if others pls specify / Others
A3.5	What type of toilet facility does this house have?	1.Use open Space 2.Bucket 3.Flush latrine 4.Close pit 5.Public Latrine; 6.Other plese specify — if others pls specify / Others
A3.6	Does this house have a seprate Kitchen	1.Yes,seprate 2.No, in a living room; 3.No,in an open verandah; 4.No,in an open space
A3.7	Does this house have electricity	○ Y ○ N
A3.8	Does this house have a sui gas connection	○ Y ○ N

A3.9	Does this household have/own any of the following.	
A3.9a	Refrigerator	○ Y ○ N
A3.9b	TV (Color)	○ Y ○ N
A3.9c	TV (Black & White)	○ Y ○ N
A3.9d	Dish Antenna/Cable	○ Y ○ N
A3.9e	Washing machine	○ Y ○ N
A3.9f	Telephone	○ Y ○ N
A3.9g	Computer	○ Y ○ N
A3.9h	Scooter/Motor cycle	○ Y ○ N
A3.9i	Car/Suzuki/jeep/van	○ Y ○ N

Income Range

A3.10	Kindly provide information on all kinds of income to this household.	
A3.10a	During Last MONTH	
A3.10b	During Last YEAR	

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B1 Personal Medical History

اس حصہ میں، میں آپ سے آپ کی صحت کے متعلق پوچھوں گا/ گی۔

B1.1	کیا آپ سے کبھی کسی ڈاکٹر نے بتایا ہائی بلڈ پریشر چیک کروایا ہے؟ باقی بلڈ پریشر اگر نہیں تو سوال نمبر B1.5 پر جائیں۔	○ Y ○ N
B1.2	کیا آپ کو کبھی معالج نے بتایا ہے کہ آپ کو ہائی بلڈ پریشر کی بیماری ہے؟ اگر نہیں تو، سوال نمبر B1.5 پر جائیں۔	○ Y ○ N
B1.3	اس وقت آپ کی عمر کیا تھی جب آپ کو بتایا گیا کہ آپ کو ہائی بلڈ پریشر ہے؟	☐☐
B1.4	ہائی بلڈ پریشر کی وجہ سے آپ کے معالج نے کبھی آپ کو تجویز کردہ دوائی استعمال کرنے کے لئے کہا؟	○ Y ○ N
B1.5	**دل کی بیماری** کیا آپ کو کبھی کسی معالج نے بتایا ہے کہ آپ کو دل کی بیماری ہے؟ اگر نہیں تو، سوال نمبر B1.10 پر جائیں۔	○ Y ○ N ○ DK
B1.6	وہ دل کی بیماری کیا تھی؟ Others ☐☐	○ Heart Attack ○ Angina ☐☐☐☐☐☐☐☐☐☐
B1.7	جب آپ کو بتایا گیا کہ آپ کو دل کی بیماری ہے تو اس وقت آپ کی عمر کیا تھی؟	☐☐
B1.8	کیا اس کیلئے آپ کو کوئی دوا تجویز کی گئی؟	○ Y ○ N
B1.9	اگر ہاں، تو علاج کی نوعیت کیا تھی؟	○ میڈیکل ○ میڈیکل اور سرجیکل
B1.10	کیا آپ کو کبھی معالج نے بتایا ہے کہ آپ کو گردوں کی بیماری ہے؟ گردوں کی بیماری اگر نہیں تو، سوال نمبر B1.14 پر جائیں۔	○ Y ○ N ○ DK
B1.11	جب آپ کو بتایا گیا کہ آپ کو گردوں کی بیماری ہے تو اس وقت آپ کی عمر کیا تھی؟	☐☐
B1.12	کیا اس کیلئے آپ کو کوئی دوا تجویز کی گئی؟ اگر نہیں تو، سوال نمبر B1.14 پر جائیں۔	○ Y ○ N
B1.13	اگر ہاں، تو علاج کی نوعیت کیا تھی؟	○ میڈیکل ○ میڈیکل اور سرجیکل
B1.14	کیا آپ کو کبھی کسی معالج نے بتایا ہے کہ آپ کو شوگر کی بیماری ہے؟ ذیابیطس اگر نہیں تو، سوال نمبر B1.19 پر جائیں۔	○ Y ○ N ○ DK ○ Had Symptoms ○ Screening only
B1.15	آپ کو کیسے شک ہوا کے آپ کو شوگر کی بیماری ہے؟ Others ☐☐	☐☐☐☐☐☐☐☐☐☐
B1.16	جب آپ کو بتایا گیا کہ آپ کو شوگر کی بیماری ہے تو اس وقت آپ کی عمر کیا تھی؟	☐☐
B1.17	کیا اس کیلئے آپ کو کوئی دوا تجویز کی گئی؟	○ Y ○ N
B1.18	اگر ہاں، تو کون سی دوا؟ Others ☐☐	☐ Insulin ☐ Tablets ☐ Diet only ☐☐☐☐☐☐☐☐☐☐
B1.19	کیا آپ کو کبھی فالج کا اٹیک/ حملہ ہوا ہے؟ فالج اگر نہیں تو، سوال نمبر B1.22 پر جائیں۔	○ Y ○ N
B1.20	جب آپ کو بتایا گیا کہ آپ کو فالج کا حملہ ہوا ہے تو اس وقت آپ کی عمر کیا تھی؟	☐☐
B1.21	کیا اس کیلئے آپ کو کوئی دوا تجویز کی گئی؟	○ Y ○ N
B1.22	کیا آپ آجکل کوئی دوائی استعمال کر رہے ہیں؟	○ Y ○ N
B1.23	آپ کس بیماری کے لیے دوا لے رہے ہیں؟	☐ BP ☐ CVD ☐ Diabetics ☐ Cholestrol ☐ Other
B1.24	کیا آپ کو کسی معالج نے بتایا کے آپ کو دمہ یا پھیپھڑوں کی بیماری ہے؟ ○ Y ○ N	پھیپھڑوں کی بیماری ☐ دمہ ☐ اگر ہاں تو کون سی؟

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B2 Family Medical History

B2.1	اپ کی عمر کیا ہے؟	☐☐
B2.2	اگر اپ شادی شدہ ہے، تو کیا اپ کی بیوی/شوہر اپ کے (First Cousin) ہے؟	○ Y ○ N ○ NA
	ہائی بلڈ پریشر	
B2.3	کیا آپ کے قریبی خاندان کے کسی بھی فرد کو کبھی معالج نے بتایا ہے کہ اسے ہائی بلڈ پریشر کی بیماری ہے؟ *(If No or Don't know, skip to B2.5)*	○ Y ○ N ○ DK
B2.4	اگر ہاں تو کس کو؟	☐ والدین ☐ بہائی/بہن ☐ بچے
	دل کی بیماری	
B2.5	کیا آپ کے قریبی خاندان کے کسی بھی فرد کو کبھی معالج نے بتایا ہے کہ اُسے دل کی تکلیف یا ہارٹ اٹیک ہوا ہے؟ *(If "No" or "Don't Know" skip to B2.7)*	○ Y ○ N ○ DK
B2.6	اگر ہاں تو کس کو؟	☐ والدین ☐ بہائی/بہن ☐ بچے
	ذیابیطس	
B2.7	کیا آپ کے قریبی خاندان کے کسی بھی فرد کو کبھی معالج نے بتایا ہے کہ اُسے شوگر کی بیماری ہے؟ *(If "No" or "Don't Know" skip to B2.9)*	○ Y ○ N ○ DK
B2.8	اگر ہاں تو کس کو؟	☐ والدین ☐ بہائی/بہن ☐ بچے
	فالج	
B2.9	کیا آپ کے قریبی خاندان کے کسی بھی فرد کو کبھی معالج نے بتایا ہے کہ اُسے فالج کا حملہ ہوا ہے؟ *(If "No" or "Don't Know" skip to B2.11)*	○ Y ○ N ○ DK
B2.10	اگر ہاں تو کس کو؟	☐ والدین ☐ بہائی/بہن ☐ بچے
B2.11	کیا آپ کی والدہ ابھی حیات ہیں؟	○ Y ○ N
	اگر نہیں تو سوال نمبر B2.14 پر جائیں	
B2.12	جب آپ کی والدہ کا انتقال ہوا تب ان کی عمر کیا تھی؟	☐☐
B2.13	ان کے انتقال کی وجہ کیا تھی؟	☐ دل کا دورہ ☐ فالج ☐ کینسر ☐ ذیابیطس ☐ پتہ نہیں
	Others ☐☐	☐☐☐☐☐☐☐☐☐☐
B2.14	کیا آپ کی والد ابھی حیات ہیں؟	○ Y ○ N
	اگر نہیں تو سوال نمبر B3 پر جائیں	
B2.15	جب آپ کے والد کا انتقال ہوا تب ان کی عمر کیا تھی؟	☐☐
B2.16	ان کے انتقال کی وجہ کیا تھی؟	☐ دل کا دورہ ☐ فالج ☐ کینسر ☐ ذیابیطس ☐ پتہ نہیں
	Others ☐☐	☐☐☐☐☐☐☐☐☐☐

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B3 Tobacco Use

	سگریٹ / سگار / بیڑی	
B3.1	کیا آپ نے اپنی زندگی میں کبھی سگریٹ / سگار / بیڑی پی ہے؟ (اگر نہیں تو سوال نمبر B3.9 پر جائیں)	○ Y ○ N
B3.2	آپ نے کس عمر میں سگریٹ / سگار / بیڑی پینا شروع کی؟	☐☐
B3.3	کیا آپ آج کل سگریٹ / سگار / بیڑی پیتے ہیں؟ (اگر نہیں تو سوال نمبر B3.6 پر جائیں)	○ Y ○ N
B3.4	اوسطاً آپ دن میں کتنی سگریٹ / سگار / بیڑی پیتے ہیں؟	☐☐
B3.5	کیا یہ سگریٹ / سگار / بیڑی فلٹر والے یا بغیر فلٹر والے ہوتے ہیں؟ (اب آپ سوال نمبر B3.9 پر جائیں)	○ Filter ○ Non Filter
B3.6	اوسطاً آپ ایک دن میں کتنی سگریٹ / سگار / بیڑی پیا کرتے تھے؟	☐☐
B3.7	آپ نے کس عمر میں سگریٹ / سگار / بیڑی پینا چھوڑ دی؟	☐☐
B3.8	آپ نے سگریٹ / سگار / بیڑی پینا کیوں چھوڑ دی؟	☐☐☐☐☐☐☐☐
	حقہ / پائپ	
B3.9	کیا آپ نے اپنی زندگی میں کبھی حقہ / پائپ پیا ہے؟ (اگر نہیں تو سوال نمبر B3.16 پر جائیں)	○ Y ○ N
B3.10	آپ نے کس عمر میں حقہ / پائپ پینا شروع کیا؟	☐☐
B3.11	کیا آپ آج کل حقہ / پائپ پیتے ہیں؟ (اگر نہیں تو سوال نمبر B3.13 پر جائیں)	○ Y ○ N
B3.12	اوسطاً آپ ایک ہفتے میں کتنا تمباکو استعمال کرتے ہیں؟ (اب آپ سوال نمبر B3.16 پر جائیں)	☐☐☐☐ gms
B3.13	اوسطاً آپ ایک ہفتے میں کتنا تمباکو استعمال کرتے تھے؟	☐☐☐☐ gms
B3.14	آپ نے کس عمر میں حقہ / پائپ پینا چھوڑا؟	☐☐
B3.15	آپ نے حقہ / پائپ پینا کیوں چھوڑا؟	☐☐☐☐☐☐☐☐
	نسوار	
B3.16	کیا آپ نے اپنی زندگی میں کبھی نسوار استعمال کی ہے؟ (اگر نہیں تو سوال نمبر B3.23 پر جائیں)	○ Y ○ N
B3.17	آپ نے کس عمر میں نسوار استعمال کرنا شروع کی؟	☐☐
B3.18	کیا آپ آج کل نسوار استعمال کرتے ہیں؟ (اگر نہیں تو سوال نمبر B3.20 پر جائیں)	○ Y ○ N
B3.19	اوسطاً آپ ایک دن میں کتنی مرتبہ نسوار استعمال کرتے ہیں؟ (اب آپ سوال نمبر B3.23 پر جائیں)	☐☐
B3.20	اوسطاً آپ ایک دن میں کتنی نسوار استعمال کرتے تھے؟	☐☐☐☐ gms
B3.21	آپ نے کس عمر میں نسوار کا استعمال چھوڑا؟	☐☐
B3.22	آپ نے نسوار کا استعمال کیوں چھوڑا؟	☐☐☐☐☐☐☐☐
	پان یا بغیر پان تمباکو چبانا	
B3.23	کیا آپ نے اپنی زندگی میں کبھی پان یا بغیر پان تمباکو چبایا ہے؟ (اگر نہیں تو سوال نمبر B4.1 پر جائیں)	○ Y ○ N
B3.24	آپ نے کس عمر میں پان یا بغیر پان تمباکو چبانا شروع کیا؟	☐☐
B3.25	کیا آپ آج کل پان یا بغیر پان تمباکو چباتے ہیں؟ (اگر نہیں تو سوال نمبر B3.27 پر جائیں)	○ Y ○ N
B3.26	اوسطاً آپ ایک دن میں پان یا بغیر پان تمباکو چباتے ہیں؟ (اب آپ سوال نمبر B4.1 پر جائیں)	☐☐
B3.27	اوسطاً آپ ایک دن میں پان یا بغیر پان تمباکو چباتے تھے؟	☐☐☐☐ gms
B3.28	آپ نے کس عمر میں پان یا بغیر پان تمباکو چبانا چھوڑا؟	☐☐
B3.29	آپ نے پان یا بغیر پان تمباکو چبانا کیوں چھوڑا؟	☐☐☐☐☐☐☐☐

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B4 Personal Diet

اب میں آپ سے مختلف کھانوں کے بارے میں پوچھوں گا/ گی، اور میں چاہوں گا/ گی کہ آپ مجھے ایک بار بتائیں کہ کتنی مرتبہ یہ کھانے ایک دن میں، ہفتے میں یا مہینے میں کھاتے ہیں یا پھر کبھی کبھار/ کبھی نہیں کھاتے۔

No.	FOOD Items	کبھی نہیں	مہینہ /	ہفتہ /	دن /
B4.1	انڈا	☐	☐☐	☐☐	☐☐
B4.2	پراٹھا	☐	☐☐	☐☐	☐☐
B4.3	تندوری نان	☐	☐☐	☐☐	☐☐
B4.4	حلوہ پوری	☐	☐☐	☐☐	☐☐
B4.5	دودھ بالائی کے ساتھ	☐	☐☐	☐☐	☐☐
B4.6	دودھ بغیر بالائی کے ساتھ	☐	☐☐	☐☐	☐☐
B4.7	بالائی یا ملائی	☐	☐☐	☐☐	☐☐
B4.8	میٹھا مثلاً کسٹرڈ، کھیر، فرنی وغیرہ	☐	☐☐	☐☐	☐☐
B4.9	آئس کریم	☐	☐☐	☐☐	☐☐
B4.10	دہی	☐	☐☐	☐☐	☐☐
B4.11	میٹھی لسی	☐	☐☐	☐☐	☐☐
B4.12	نمکین لسی	☐	☐☐	☐☐	☐☐
B4.13	مارجرین	☐	☐☐	☐☐	☐☐
B4.14	مکھن	☐	☐☐	☐☐	☐☐
B4.15	بکرے کا گوشت (سالن، روسٹ وغیرہ)	☐	☐☐	☐☐	☐☐
B4.16	گائے کا گوشت (سالن، روسٹ، کباب، قیمہ وغیرہ)	☐	☐☐	☐☐	☐☐
B4.17	مرغی (سالن، روسٹ، تکہ وغیرہ)	☐	☐☐	☐☐	☐☐
B4.18	مچھلی (سالن، فرائی وغیرہ)	☐	☐☐	☐☐	☐☐
B4.19	جھینگے	☐	☐☐	☐☐	☐☐
B4.20	مغز، کلیجی، گردے وغیرہ	☐	☐☐	☐☐	☐☐
B4.21	باہر سے خریدے ہوئے کھانے مثلاً کٹلٹ، کڑاہی، نہاری، برگر، پیزا وغیرہ	☐	☐☐	☐☐	☐☐
B4.22	پکی ہوئی سبزیاں (آلو شامل نہیں)	☐	☐☐	☐☐	☐☐
B4.23	آلو (بشمول دوسری سبزیوں اور گوشت)	☐	☐☐	☐☐	☐☐
B4.24	کچی سبزیاں (سلاد وغیرہ)	☐	☐☐	☐☐	☐☐
B4.25	بریانی، پلاؤ	☐	☐☐	☐☐	☐☐
B4.26	دالیں، لوبیا، مٹر وغیرہ	☐	☐☐	☐☐	☐☐
B4.27	پھل (جوس شامل نہیں)	☐	☐☐	☐☐	☐☐
B4.28	تازہ پھلوں کے جوس (پیکٹ کے جوس شامل نہیں)	☐	☐☐	☐☐	☐☐
B4.29	بیکری کی اشیاء (کیک، پیسٹری، بسکٹ وغیرہ)	☐	☐☐	☐☐	☐☐
B4.30	میٹھائی، حلوہ	☐	☐☐	☐☐	☐☐
B4.31	نمکین اور تلی ہوئی اشیاء مثلاً آلو چپس، پکوڑے، سموسہ، نمکو، پاپ کارن وغیرہ	☐	☐☐	☐☐	☐☐
B4.32	مونگ پھلی، بادام، چلغوزہ، اخروٹ وغیرہ	☐	☐☐	☐☐	☐☐
B4.33	چاکلیٹ و دیگر ٹافیاں	☐	☐☐	☐☐	☐☐
B4.34	کوئی اور ایسی اشیاء جو آپ استعمال کرتے ہو اور ہم نے نہ پوچھی ہو۔	☐	☐☐	☐☐	☐☐

Countined.....

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B6 Physical Activity

ہم ان جسمانی کاموں کے بارے میں جاننا چاہتے ہیں جو لوگ روزمرہ زندگی میں انجام دیتے ہیں۔ ہم آپ سے پچھلے ے دنوں کے بارے میں سوالات پوچھیں گے آپ ان جسمانی کاموں یا مشقت کے بارے میں سوچیں جو کہ آپ نے اپنے کام، گھر کے کام، ایک جگہ سے دوسری جگہ آنے جانے کے سلسلے میں اور اپنے فارغ وقت میں سیر و تفریح، ورزش یا کھیل کود کے دوران کام کیے ہوں۔ آپ اُن تمام سخت مشقت والے کاموں کے بارے میں سوچیں جو کہ آپ نے پچھلے سات دنوں میں کئے ہوں۔ وہ سارے کام کاج جن کے کرنے سے آپکی سانس کی رفتار معمول سے بہت زیادہ تیز ہوجائے، سخت جسمانی مشقت میں آتے ہیں۔ ان کاموں کے بارے میں سوچیں جو آپ نے کم از کم 10 منٹ تک کئے ہوں۔

B6.1 گزشتہ 7 دنوں کے دوران آپ نے کتنے دن سخت مشقت والے کام کئے ہیں جیسا کہ وزنی سامان اُٹھانا، کھدائی کرنا، ورزش کرنا یا تیز رفتاری سے سائیکل چلانا۔ (اگر نہیں تو سوال نمبر B6.3 پر جائیں)

دن ہفتہ میں ☐
☐ No virgorous phsical activity

B6.2 اُن دنوں کے دوران آپ نے عموماً ایک دن میں کتنا وقت سخت جسمانی محنت والے کاموں میں صرف کیا۔

گھنٹے دن میں ☐☐
منٹ دن میں ☐☐
☐ Not sure/DK

اب آپ گزشتہ 7 دنوں کے دوران درمیانی مشقت والے کاموں یا مصروفیات کے بارے میں سوچیں۔ درمیانی مصروفیات سے مراد وہ مصروفیات ہیں جس میں درمیانی جسمانی مشقت لگتی ہو اور آپ کو معمول سے کچھ زیادہ زور سے سانس لینی پڑے۔ آپ صرف اُن جسمانی مصروفیات کے بارے میں سوچیں جو کہ آپ نے ایک وقت میں کم سے کم ۱۰ منٹ کے لئے کی ہو۔

B6.3 گزشتہ 7 دنوں کے دوران آپ نے کتنے دن درمیانہ مشقت والے کام کئے جیسا کہ ہلکا وزن اُٹھانا، عام رفتار سے سائیکل چلانا، بچوں کو گود میں اُٹھانا، پانی کا گھڑا یا باٹلی ایک جگہ سے دوسری جگہ لے جانا، اس میں چہل قدمی (ٹہلنا) شامل نہ کریں۔ (اگر نہیں تو سوال نمبر B6.5 پر جائیں)

دن ہفتہ میں ☐
☐ No moderate Phy actv

B6.4 اُن دنوں میں آپ نے عموماً کتنا وقت ان درمیانہ مشقت والے کاموں میں صرف کئے۔

گھنٹے دن میں ☐☐
منٹ دن میں ☐☐
☐ Not sure/DK

اب آپ گزشتہ 7 دنوں کے دوران اُس وقت کے بارے میں سوچیں جو کہ آپ نے چہل قدمی میں صرف کیا۔ اس میں شامل ہے گھر اور نوکری، ایک جگہ سے دوسری کا سفر اور کوئی اور چہل قدمی (ٹہلنا) جو کہ آپ نے صرف تفریح، کھیل، ورزش یا راحت و آرام کے لئے کی ہو۔

B6.5 گزشتہ 7 دنوں کے دوران آپ نے کتنے دن کم از کم ایک وقت میں 10 منٹ تک چہل قدمی کی۔ (اگر نہیں تو سوال نمبر B6.7 پر جائیں)

دن ہفتہ میں ☐
☐ No walking

B6.6 ان دنوں میں آپ نے عموماً کتنا وقت چہل قدمی میں صرف کیا۔

یہ سوال اُس وقت کے متعلق ہے جو گزشتہ 7 دنوں کے دوران کام کے دنوں میں آپ نے بیٹھنے میں صرف کیا ہو اس میں شامل کریں وہ وقت جو کہ آپ نے صرف کیا ہو کام یا نوکری میں، گھر پر اور راحت اور آرام کے دوران، اس میں وہ وقت بھی شامل ہو سکتا ہے جو صرف کیا ہو ڈیسک پر بیٹھنے میں، دوستوں سے ملنے میں، پڑھنے میں، بیٹھ کر یا لیٹ کر ٹی وی دیکھنے میں۔

گھنٹے دن میں ☐☐
منٹ دن میں ☐☐
☐ Not sure/DK

B6.7 گزشتہ 7 دنوں میں آپ نے کام کے دنوں میں کتنا وقت بیٹھ کر گزارا۔

گھنٹے دن میں ☐☐
منٹ دن میں ☐☐
☐ Not sure/DK

B6.8 اوسطاً آپ نے ایک ہفتے میں کتنے دن گھر یا گھر کے باہر درج ذیل کاموں میں گزارے؟
(اگر کوئی کام نہ کیا ہو تو جواب میں "0" لکھیں اور اگر جواب "0" نہ ہو تو گھنٹوں کے بارے میں پوچھیں)۔

کام	نمبر	days/week	hours/day
کھانا پکانا	1	☐	☐☐
گھر کی صفائی مثلاً پونچا، جھاڑو وغیرہ لگانا۔	2	☐	☐☐
کپڑے دھونا اور استری کرنا۔	3	☐	☐☐
خریداری کرنا اور گھر کے لئے سودا لے کر آنا۔	4	☐	☐☐

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C1 Anthropometry and BP Readings

	1t Reading Time: _____	
C1.1	Have you smoked a cigarette or taken coffee or tea in the last 30 minutes?	○ Yes ○ N
C1.2	Mid arm circumference	☐☐☐ cm
C1.3	Cuff size	○ Larger ○ Extra-Larger
C1.4	Pulse (Right forearm)	☐☐☐ /min
C1.5	Systolic Blood pressure (Right arm)	☐☐☐ mmHg
C1.6	Diastolic Blood pressure (Right arm)	☐☐☐ mmHg
	2nd reading after 01 minutes	
C1.7	Pulse (Right forearm)	☐☐☐ /min
C1.8	Systolic Blood pressure (Right arm)	☐☐☐ mmHg
C1.9	Diastolic Blood pressure (Right arm)	☐☐☐ mmHg
	3rd reading after 01 minutes	
C1.10	Pulse (Right forearm)	☐☐☐ /min
C1.11	Systolic Blood pressure (Right arm)	☐☐☐ mmHg
C1.12	Diastolic Blood pressure (Right arm)	☐☐☐ mmHg
	Mean of Final 02 readings	
C1.13	Mean Systolic Blood pressure	☐☐☐ mmHg
C1.14	Mean Diastolic Blood pressure	☐☐☐ mmHg

Anthropometric measurement

C1.15	Height ----------	☐☐☐.☐ cm
C1.16	Weight ----------	☐☐☐.☐ Kg
C1.17	Hip circumference ----------	☐☐☐.☐ cm
C1.18	Waist circumference ----------	☐☐☐.☐ cm

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C2 Laboratory Tests

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C2.1 Fasting Glucose	
C2.2 Triglycerides	
C2.3 Cholestrol	
C2.4 HDL	
C2.5 LDL	
C2.6 AST	
C2.7 Urine Protiens	○ YES ○ NO
C2.8 Urine Microalbumin	
C2.9 Insulin	
C2.10 CRP	

CORRECTIONS

Form	Question	Correction

CODE PAGE FINAL CODE PAGE 2/23/2005

LANGUAGE	
1	Sindhi
2	Balochi
3	Jadgal
4	Brohi
5	Gujrati
6	Memoni
7	Kathiawari
8	Urdu
9	Punjabi
10	Pushto
11	Hindko
12	Saraiki
13	Others
99	DontKnow

Ethnic Code	
1	Sindhi
2	Balochi
3	Jadgal
4	Brohi
5	Gujrati
6	Memon
7	Kathiawari
8	Muhajir
9	Punjabi
10	Pushtoon
11	Hindko
12	Saraiki
13	Others
99	DontKnow

Relation to HH	
1	Self
2	Spouse
3	Son/Daughter
4	Son-in-Law/Daughter-in-Law
5	Grandson/ Granddaughter
6	Parent
7	Sibling
8	Other Relative
9	Other Non relative

Highest Education Level	
1	Illiterate
2	Madressa
3	Primary
4	Secondary
5	Matriculation
6	Intermidiate
7	Bachelors
8	Masters or Above
9	DontKnow

Martial Status	
1	Married
2	Divorced
3	Seperated
4	Widowed
5	Single

Employment Status	
1	Student / Too Young
2	Working for Daily Wages(cash or Kind)
3	Self-Employed
4	Working for wages and Employed
5	Unemployed
6	Physically Handicap
7	Bed-ridden
9	DontKnow

Birth Place	
1	Lyari
2	North Nazimabad
3	Karachi
4	Sindh
5	Balochistan
6	Punjab
7	NWFP
8	Northern Areas
9	British India
10	Iran
11	Afghanistan
12	Other
99	DontKnow

Delivery Location	
1	Home, unassisted
2	Home,Dai
3	Home,Trained Attendant
4	Maternity Home
5	Hospital
6	Other
9	DontKnow

Source of Treatment	
1	No treatment
2	Govt Hospital
3	Govt Dispensary
4	Pvt Hospital
5	GP
6	Homeo
7	Hakim

Who Told You the Cause of Death	
1	Doctor
2	Other Health Person
3	Self Judgement
9	Don't Know

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Approval of Local Ethics Committee

REVIEW AND APPROVAL OF PREVALENCE OF DIABETES AND ASSOCIATED RISK FACTORS AMONG ADULTS 25 YEARS AND ABOVE IN URBAN KARACHI

By INSTITUTIONAL REVIEW BOARD

A: INFORMATION

Name and Address of Ethical Review Board:
Institutional Review Board
Baqai Institute of Diabetology and Endocrinology, III- B, 3/17, Nazimabad No. 3, Karachi- 74600

Study Title:
'Prevalence of Diabetes and Associated Risk Factors among Adults 25 Years and Above in Urban Karachi'.

Name and Address of the Principal Investigator:
Prof A. Samad Shera TI, SI, FRCP
Honorary President IDF
Director WHO Collaborating Centre
Secretary General DAP
5-E/3, Nazimabad, Karachi-74600
Ph: + 92-21-6616890 Email: dapkhi@cyber.net.pk

B: REVIEW

The following items have been reviewed in connection with the above study to be conducted by the above investigator:

Protocol
Informed Consent Document
Questionnaire / Patient Information Sheet

Conditionally approved (specify required modification here or in accompanying letter):

1. Final Questionnaire to be submitted in local language 'Urdu' before start of study.
2. Consent Form in Local Language 'Urdu'.

Date of IRB Approval: June 9, 2004

Dr. Shakil Baig
Chairman,
Institutional Review Board

INSTITUTIONAL REVIEW BOARD MEMBERS

Name	Profession	Address/Ph #
1. Dr. Shakil Baig M.B.B.S., M.R.C.P.	Consultant Rheumatologist	
2. Dr. Abdul Basit M.B.B.S., M.R.C.P.	Consultant Diabetologist & Endocrinologist	Baqai Institute of
3. Dr. Yakoob Ahmedani M.B.B.S.,FCPS	Consultant Physician	Diabetology and
4. Dr.Mohiuddin Waseem M.B.B.S,D.A.B.I.M.	Consultant Diabetologist & Endocrinologist	Endocrinology
5. Dr M Zafar Iqbal Abbasi	Administrator BIDE	Ph.: 6617234-5
6. Mufti Fazal Karim	Non-Organizational Member / Non-Medical Member	