Journal of Population Therapeutics &Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/jptcp.v30i17.2699

THE GENDER-ORIENTED PERSPECTIVE IN THE DEVELOPMENT OF TYPE 2 DIABETES MELLITUS COMPLICATIONS; SGOP STUDY.

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Abstract:
The SGOP study examines gender and ethnic differences in micro- and macrovascular complications of type 2 diabetes (T2DM). It aims to create gender-specific preventative and care methods to improve renal and cardiovascular outcomes**.** The observational study follows individuals with T2DM over time, ensuring representation of multiple genders and ethnicities. Data is obtained through medical records, interviews, and physical tests, focusing on micro- and macro-vascular problems. In our study the majority patients were male and Urdu speakers, with 30.66% having diabetes for less than 5 years and 37.66% for 5–10 years. Symptoms included polyuria, dyspnea, diarrhea, visual disruption, chest discomfort, unhealed wounds, erectile dysfunction, dyspepsia, hypertension, ischemic heart disease, and chronic liver disease. The ankle brachial index was normal for 57.33% of patients, with vascular disease detected in 15%. Fundoscopy findings showed normal findings in 50.66% of patients, with mild diabetic retinopathy identified in 37.33%.The study reveals a significant relationship between gender and HbA1c levels, ankle brachial index, and fundoscopy findings. However, in our study gender has no significant link with urine albumin-to-creatinine ratio (ACR) values. The study emphasizes monitoring and managing diabetes-related complications and identifying areas of focus for healthcare providers.It emphasizes the need for genderspecific preventative and care measures, enabling healthcare practitioners to tailor interventions, implement early detection techniques, and optimize patient care for better outcomes.

Keywords: Gender-oriented perspective; Type 2 diabetes mellitus (T2DM); microvascular and macrovascular complications; Renal and cardiovascular outcomes; AI

Introduction:

Type 2 diabetes is a metabolic disorder caused by a relative lack of insulin, often known as insulin resistance [1]. Insulin is a hormone generated by the pancreas to regulate glucose levels; however, in type 2 diabetes, the body's cells develop resistance to it or the pancreas fails to produce enough. Polyuria (excessive urination), polyphagia (increased appetite), and polydipsia (excessive thirst) are symptoms typically associated with type 2 diabetes [2]. The body attempts to remove excess glucose through increased urine production, resulting in a lack of energy. Diabetes is becoming more common worldwide, affecting people of all geographical, ethnic, and racial backgrounds [3]. Diabetes mellitus (including type 1 and type 2) impacted about 422 million people globally in 2014, according to World Health Organisation (WHO) estimates [4]. If current trends continue, the disease's burden is likely to rise, with more than 629 million individuals aged 20 to 79 expected to have diabetes by 2045 [5]. Type 2 diabetes is associated with microvascular and macrovascular problems, such as diabetic retinopathy, nephropathy, and neuropathy, which can lead to heart disease, stroke, and peripheral artery disease. [6].

Individuals with type 2 diabetes must have regular monitoring and medical care to avoid complications and preserve optimal health. Cardiovascular diseases (CVD) are one of the most common consequences of diabetes, and they are associated with greater rates of death and morbidity [7]. Type 2 diabetes is more common in obese people, which can be related to factors such as greater urbanisation and sedentary lifestyles. However, it is crucial to highlight those genetics also play a role in the development of diabetes [8]. Diabetes is becoming more common in South Asia, with type 2 diabetes affecting more than 85% of the population. In addition, people in Pakistan are more likely to develop diabetes at an earlier age [9]. This shows that genetic and environmental variables may be contributing to the high prevalence and early development of diabetes in this community. Diabetes prevalence varies by ethnic group in the United Kingdom. Minority ethnic groups are more likely than white British people to have diabetes [10]. This discrepancy may be impacted by a variety of factors, including genetic predisposition, cultural factors, and lifestyle and dietary variances.
A HELIUS study from the Netherlands adds to the evidence that ethnic minorities experience disadvantages in the development of nephropathy and coronary heart disease [11]. According to the study, ethnic minorities may have greater rates of nephropathy and coronary heart disease than the general population, implying that there may be health disparities depending on ethnicity. Men had a higher incidence of severe microalbuminuria than women, according to studies on gender differences in the development of microvascular disorders [12]. According to one study, men had a higher occurrence of microvascular problems, such as severe microalbuminuria, than women. Microalbuminuria is an early indicator of kidney impairment caused by the presence of a small amount of protein in the urine. Diabetes is diagnosed by high blood glucose levels, an oral glucose tolerance test, and abnormal glycosylated haemoglobin levels [13]. These tests will help identify whether a person has diabetes or prediabetes.

Type 2 diabetes is largely preventable by adopting a healthy lifestyle [14]. Maintaining a balanced diet, engaging in regular physical activity, managing weight, avoiding smoking, and limiting alcohol intake can all significantly reduce the risk of developing type 2 diabetes. Those who have diabetes and are unable to control it with diet and exercise should start taking medication [15]. Patients may need to take medicine to control their blood glucose levels and avoid complications from the disease. According to research, males are more likely to develop peripheral arterial disease (PAD) in individuals with diabetes due to their higher smoking prevalence. Different atherogenic risk factors may play a role in the development of PAD in diabetic women. Female sex has been recognised as a risk factor for retinopathy and/or maculopathy, while males appear to have a higher prevalence of peripheral neuropathy than females [16].

The purpose of this study is to look into gender and ethnic differences in the micro- and macrovascular consequences of type 2 diabetes mellitus (T2DM). The findings of this study are expected to support the development of gender-specific prevention and management methods, resulting in improved renal and cardiovascular outcomes for people with T2DM. The current study will expand on earlier findings by investigating additional gender and racial inequalities in T2DM micro- and macrovascular problems. The findings of this study can serve to improve understanding of chronic problems in T2DM and contribute to better renal and cardiovascular outcomes for people with the condition.

METHODS AND MATERIALS

The study is designed as an observational cohort study, involving a group of people with T2DM throughout time to assess the development of micro- and macrovascular issues.

Participant Selection: Participants were drawn from a varied community, including people of different genders and ethnic origins. To ensure adequate representation of each group, the sample size should be set based on statistical power calculations.

Data Collection: Data on gender, ethnicity, and clinical features are collected from participants. These are medical records, interviews, and physical examinations. Body mass index (BMI), blood glucose levels, lipid profiles, blood pressure, and medication history are all clinically relevant characteristics.
Microvascular issues such as retinopathy, nephropathy, and neuropathy are evaluated using ophthalmologic tests and imaging modalities. Macrovascular issues such as coronary heart disease and peripheral arterial disease (PAD) are evaluated using medical records. Gender and ethnic disparities in the prevalence of microvascular and macrovascular diseases are investigated using statistical methods. Ethical considerations are followed, and all participants give their informed consent.

Limitations and future directions are noted. The study's goal is to provide insights into gender and ethnic disparities in the micro- and macrovascular repercussions of T2DM, which can help us develop gender-specific prevention and management methods and enhance renal and cardiovascular outcomes. The research was carried out at the Dr. Ruth KM Pfau Civil Hospital's Medical Department and the Dow University Hospital Ojha Campus, DUHS Karachi's Medical Department.

RESULTS:

In our study, we discovered that 11.66% (35) of patients were between the ages of 20 and 40, 45.66% (137) were between the ages of 40 and 50, 35% (105) were between the ages of 50 and 60, and 7.66% (23) were over the age of 60. Males made up 60.33% (181) of the population studied, while females made up 39.66% (119). Urdu speakers made up 45.67% (137) , Sindhi 15.66% (47) , Pashto 23%(69) , Punjabi 9%(27), and others, including Afghani, Bengali and Kashmiri, made up 6.66% (20). Our patients had diabetes for less than 5 years in 30.66% of cases, 5–10 years in 37.66%, and more than 10 years in 31.66%.

Polyuria was identified in 31.66% (95) of our patients, polyphagia in 1% (3), dyspnoea in 44.33% (134), diarrhoea in 28.33% (85), and a history of visual disruption in 53% (159). A history of chest discomfort was discovered in 12% (36) of the cases, an unhealed wound in 13.66% (41), an ED in 20.66% (62), a history of dyspepsia in 49.66% (149) of the cases, hypertension in 56.66% (170), an IHD history in 22.33% (67), and chronic liver disease in 11.66% (35). Our 10% (30) patients had a history of COPD, 29.66% (89) had CVD, and only
1.66% (5 cases) had HIV.

ABI (ankle brachial index) was found to be normal (1.0-1.4) in 57.33% of patients (172); acceptable (0.9-1.0) in 23.66% of patients (71); some vascular disease (0.8-0.9) in 15% of patients (45); moderate arterial disease (0.5-0.8) in 4% of patients (12); and severe arterial disease (less than 0.5) in 0.33%

(1). The fundoscopy results for our patients were as follows: normal in 50.66% (152), mild NPDR in 37.33% (112), moderate NPDR in 12% (36), severe NPDR in 0.66% (2), and PDR in 0.66% (2).
The mean systolic B.P. reading was 156 mmHg, while the diastolic reading was 83 mmHg. BMI was found to range from 20.2 to 39.9, with a mean BMI of 28.02. The FBS reading varies from 277 to 333 mg/dl, the RBS reading ranges from 138 to 378 mg/dl, and the HbA1c level mean was 8.9 and ranged from 6.25 to 15.16 g%. Creatinine levels ranged from 0.26 to 3.9 mg/dl on average. The urine microalbumin mean was 79.76 mg/dl, with a range of 3 to 917 mg/dl. The mean ACR mcg/mg distribution was 74.89, with a range of 1.8 to 917. Serum cholesterol levels averaged 186.75 mg/dl and varied from 75 to 459 mg/dl. The mean TG level was 205 mg/dl, with a range of 25 to 688. HDL cholesterol levels average 37 and range from 22 to 56. The mean LDL cholesterol level was 119 mg/dl, with a range of 60 to 231.

12.66% (38) had a history of hypoglycaemia, and 18% (46) had renal impairment.
Our findings indicate that there is a significant link between sex and HbA1c levels. We may conclude from the chi-square analysis that there is a connection between gender and HbA1c levels in the cohort investigated. Compare the gender data (male and female) to the ACR mcg/mg readings while completing the chi-square analysis (χ^2). The chi-square statistic is 0.9607, and the p-value is 61856. The result is not statistically significant at p.05. Compare the sex data (male and female) with the ABI (ankle brachial index) when performing the chisquare analysis. The chi-squared value is 44.7215. The p-value is set at 0.00001. At p.05 The outcome is considerable. Compare the sex data (male and female) with the fundoscopy findings while performing the chi-square analysis (χ^2). The chi-square value is 14.4807. The significance level is.005909. At p.05 The outcome is considerable.
ANOVA analysis revealed a significant difference between groups in terms of length of DM, sex, and urine for microalbuminuria, with a significance level of 0.001. The data also show that the duration of the diabetes is statistically significant in the development of abnormal sensation and vision abnormalities, with a p-value of 0.001. At p.05. The outcome is considerable.
In conclusion, the chi-square analysis shows that there is no significant relationship between gender and ACR mcg/mg. However, there are substantial correlations between gender and HbA1c, ABI, and fundoscopy findings.

Table 1: Language Group distribution

	Total no 300	Abnormal sensation
Urdu speakers	45.67% (137)	(20.66% (37)
Sindhi	15.66% (47)	12.33% (38)
Pashto	23%(69)	12.33%(37)
Punjabi	9% (27),	4.33% (14)
Others (including Afghani, Bengali, and Kashmiri)	6.66% (20)	2.66% (8).

Table 2: Chi-square analysis (χ^2) compares the sex data (male and female) with the HbA1c readings.

	HbA1c less than 7.5	HbA1c between 7.5 to 8.5	HbA1c between more than 8.5
Males	19	36	63
Females	37	48	97

Table 3: Chi-square analysis (χ^2) compares the sex data (male and female) with the ABI (ankle brachial index)

	Normal (1.0- 1.4)	Acceptable (0.9-1.0)	Some vascular disease (0.8- 0.9)	Moderate arterial disease (0.5-0.8)	Severe arterial disease (less than 0.5)
Males	46	30	33	9	1
Females	126	41	11	2	1

Table 4: Chi-square analysis (χ^2) compares the sex data (male and female) with the Fundoscopy finding

	Normal	Mild NDPR	Moderate NDPR	Severe NDPR	PDR
Males	45	52	20	1	1
Females	107	58	14	1	1

DISCUSSION:

According to statistics from the 1999–2004 NHANES, the prevalence of microvascular problems among persons with type 2 diabetes is substantially higher than that of macrovascular complications, and they can be episodic or progressive, leading to permanent damage. It was also discovered to be related to the length of the DM. Early detection and therapeutic efforts are critical for minimising the risk of complications in people who have had diabetes for a long time [17]. Based on diabetes duration, patients were classified into three groups: approximately 30.66% had diabetes for less than 5 years, 37.66% had diabetes for 5–10 years, and 31.66% had diabetes for more than 10 years.

The most common comorbidities in T2DM patients, according to Kristy Iglay's study, were hypertension (HTN) in 82.1%, overweight or obesity in 78.2%, hyperlipidaemia in 77.2%, chronic kidney disease (CKD) in 24.1%, and cardiovascular disease (CVD) in 21.6% [18]. In our investigation, the prevalence of related illnesses such as hypertension (56.66%), dyspepsia (49.66%), chronic liver disease (11.66%), chronic obstructive pulmonary disease (10%), cardiovascular disease (29.66%), and renal impairment (18%) was shown to be substantial. These comorbidities will necessitate extensive care and multidisciplinary management, both of which are required for managing type 2 diabetes.

Table 1 shows the variation in the presence of abnormal sensations across different language groups. Urdu Speakers: Out of the 137 Urdu speakers, 37 individuals (27%) reported experiencing abnormal sensations. Sindhi speakers were 47 individuals, and 38 individuals (79%) reported abnormal sensations. Of the 69 Pashto-speaking individuals, 37 (53%) reported abnormal sensations. Among the 27 Panjabi individuals, 14 (51%) reported abnormal sensations. Of the 20 individuals from other (Afghani, Bengali, Kashmiri, etc.) language groups, 8 (40%) reported abnormal sensations.

This data highlights a significant variation in the presence of abnormal sensations across different language groups. Sindhi speakers have the highest percentage, followed by Pashto and Punjabi speakers, while individuals from other language groups and Urdu speakers have relatively lower percentages. Our findings are analogous to those of the UK Prospective Diabetes Study (UKPDS), which found ethnic differences in type 2 diabetes. Afro-Caribbean patients had a decreased risk of myocardial infarction, whereas Indian-Asian patients were more likely to develop nephropathy than white Caucasians [19].

HbA1c levels have been linked to age and gender in studies of Chinese populations. In the 30- to 59-year-old age groups, male HbA1c levels were significantly higher than female HbA1c levels (P 0.05) [20]. In our study, we found that gender and HbA1c levels were shown to be substantially associated. The chi-square analysis found a statistically significant relationship between gender and HbA1c values in the cohort investigated. Males had a mean HbA1C value of 9.0, while females had a mean HbA1C value of 8.9.

ABI was observed in 34 (68%) of the patients in a study, with male gender predominance in 22 (64.7%), and the mean SD for ABI in the male and female populations was 0.512.31 and 0.631.94, respectively [21]. Gender and ABI were found to have a significant relationship in our study [table 3]. Male patients had a higher rate of aberrant ABI readings than female patients. This disparity shows that there may be gender disparities in the development and severity of peripheral vascular disease in type 2 diabetes patients. It emphasises the significance of gender-specific risk assessment and tailored preventive strategies in reducing the risk of peripheral vascular problems.

According to a study by Mei Li, females had a higher frequency of DR than males in T2DM patients with a diabetes history of more than 10 years, ages above 60, or a usually intermediate economic status [22]. Male patients exhibited a higher prevalence of nonproliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR) than females, according to our findings [Table 4]. This emphasises the significance of regular eye exams and individualised retinopathy management approaches, as well as gender differences in the development and progression of retinopathy.
Gender data (male and female) was not statistically significant in our study when compared to ACR mcg/mg readings and urine for microalbumin levels.

Furthermore, we discovered in our study that the duration of diabetes has a statistically significant link with the development of abnormal sensations and vision abnormalities. This data also has a p-value of 0.001, demonstrating a highly significant relationship between diabetes duration and these issues. The findings indicate that there are significant differences between groups in terms of the variables evaluated (diabetes duration, sex, urine for microalbuminuria), and that diabetes duration is strongly connected with the development of abnormal sensations and vision impairments.

Smith et al. found that having diabetes for a longer period was strongly linked to an elevated risk of neuropathy and its associated symptoms. This suggests that long-term hyperglycaemia and metabolic abnormalities associated with diabetes can cause nerve damage, leading to altered emotions. Johnson et al. found that having diabetes for a longer period was linked to a higher prevalence of diabetic retinopathy, a common vision impairment among diabetics [23-27].

Our findings contribute to the existing body of information by emphasising the significance of diabetes duration in the development of abnormal sensations and vision impairments. The strong link found in our study highlights the importance of early detection and intervention approaches aimed at preventing or controlling these complications in people with diabetes for a longer period.

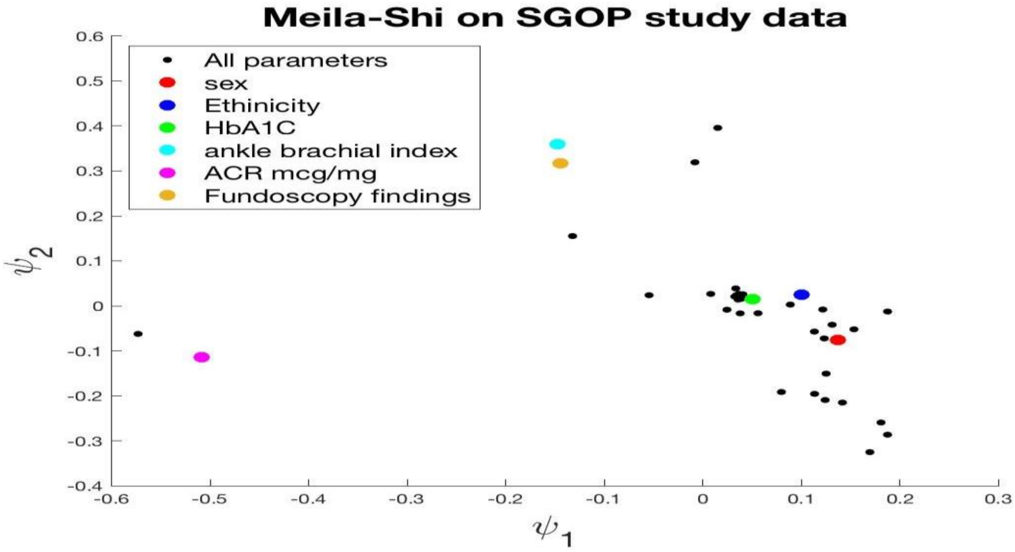
It is crucial to acknowledge that our study has significant limitations. First, the cross-sectional technique limits our ability to demonstrate a causal relationship between diabetes duration and observed issues. Longitudinal research would provide greater evidence of these variables' temporal association. Furthermore, because our research was limited to a single community, the findings may not be applicable to other ethnic or demographic groups.

Finally, our findings show that the duration of diabetes has a significant impact on the development of aberrant feelings and vision anomalies. These findings emphasise the significance of early detection, regular monitoring, and tailored therapies for people with long-term diabetes to effectively prevent or control these problems. More studies, especially prospective studies, are needed to explain the underlying mechanisms and investigate novel therapies that can ameliorate the deleterious effects of long-term diabetes on these outcomes.

Figure 1 shows the generated 2D image from a new metric shown in the appendix (Annexure 1). Each point on the 2D graphic represents one of around 40 parameters. Each parameter representing a column of the datasheet M is now reduced to a 2D point. The parameters of interest are color-coded. It should be noted that the closer two points are to each other, the closer their relationship, and the further they are from each other, the less they are linked. The result matches the chi-square analysis findings. The ACR is discovered to be an outlier in relation to most of the data parameters. The sex' parameter is discovered to be relatively central in close vicinity to HbA1C and 'ethnicity'. Ankle brachial index (ABI)'Fundoscopy Findings' are close together and appear to be part of a sub-cluster near sex'.

As we can see, the resulting clustering picture enables us to create representative focal areas for the discovery of probable relationships, which would be difficult, if not impossible, using traditional statistical analysis. This method is based on matrix algebra, and tools such as MATLAB or even Python code can handle the basic algebraic operations quickly and easily [28-30]. Annexure -1 show the further detail.

Figure 1 - 2D representation of Data parameters



CONCLUSION:

The study gives valuable insights into the patient population's characteristics and health state, emphasising the importance of continued monitoring, care, and prevention of diabetes-related problems. These findings can help healthcare practitioners customise interventions, adopt early detection measures, and optimise patient care to enhance overall diabetic outcomes.

We've also introduced a new visualisation metric that validates our statistical analysis and could be used in a variety of applications and research.

Ethical permission: Dow University of Health Sciences Karachi

Conflict of Interest: There is no conflict of interest.

Funding: This is a self-funded study.

AUTHOR CONTRIBUTIONS:

Kumar D: Contributions to conception and design, acquisition of data, analysis and interpretation of data

Kashif: Drafting the article and shares its expert opinion and experience in finalizing the manuscript

Tony: Data analysis and interpretation of data and make it suitable for final revision

Sami: Contributed to conception and interpretation of data and give expert view

Qadeer R: Final proofreading, review of literature and sequencing the material as well as grammatical review.

Anum G: Collection and acquisition of data and help in analysis and review of manuscript.

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Annexure 1 Alternative Metric from AI:

The spreadsheet data has the following features:

1. The data is a combination of continuous and discrete data, mostly codes.
2. The data is a combination of assigned integers and measurements.

Although some datasheet parameters (columns) are measurements in terms of floating-point numbers, many of the parameters, especially those pertaining to the patient personal history are codes which are integers numbers like 1,2,3.... These are man-made codes, categories of e.g., age group and true/false flags. The codes have different meanings depending in the parameter and some are somewhat subjective (e.g. age group categories can be done differently).

Now, a standard metric to assess the correlation between columns of data is the Pearson correlation coefficient defined as follows:

$$r = \frac{\sum_{i=1}^{n}(x_i - \overline{x})(y_i - \overline{y})}{\sqrt{\sum_{i=1}^{n}(x_i - \overline{x})^2(y_i - \overline{y})^2}}$$

where:

- n is the sample size,
- x_i and y_i are the individual sample points indexed with i,
- $\overline{x}$ and $\overline{y}$ are the sample means.

Technically, a Pearson coefficient is the cosine of the angle between two normalized vectors. If the individual vectors are totally different parameters, one is literally comparing apples to oranges. The Pearson coefficient is not so meaningful when
Comparing experimental measure with subjective codes. We need an alternative metric which is agnostic to the choice of coding, as much as possible.

Thus, we make use of a tried and tested spectral clustering technique used in dimensional reduction and data clustering [28,29] which exploit algorithms of computational quantum mechanics. We follow closely the example entitled 'Finding Clues of a Disease' [sec. 3.1.3,29].

We formulate the method as follows. Since we want to establish the relations between the parameters which are the column vectors of the datasheet, we define a *similarity matrix* from the data matrix *M* as follows:

$$S = Q^T \times Q$$

where T denotes the transpose operation, the cross × denotes matrix multiplication and $Q = log_2$ (M+1). This similarity matrix *S* is also the adjacency matrix representing a graph where the graph nodes are these parameters. Next, we convert the matrix *S* into a *row stochastic matrix*, called *p*:

$$p_{i,j} = {S_{i,j}}\Big/{\sum_{k=1} S_{i,k}}$$

where we divided each row of the matrix S by each respective sum of that row. The resulting matrix p is called a Markov matrix or a transition matrix in the language of quantum mechanics. We obtain both the eigenvalues and the eigenvectors of p according to:

$$p\psi = \lambda\psi$$

where ψ is the eigenvector and λ is the eigen value? This is the very mathematical basis of quantum mechanics and even some statistics. The eigenvalues of *p* have the following property:

$$\lambda_0 = 1 \text{ and } \lambda_{i+1} < \lambda_i \text{ and } i = 0,1,2,\dots$$

The zeroth eigenvalue of a row stochastic matrix in always unity and its corresponding eigenvector is a constant vector. This corresponds to the background and can be discarded. It is the variations from this constant vector represented by the next two lower eigenvalues,
λ_1 and λ_2, we want. Plotting the eigenvectors $\psi_1(\lambda_1)$ against $\psi_2(\lambda_2)$, yields a flat two dimensional (2D) picture of the data. This Visual data analysis technique gives us a clustering picture and further strengthens our interest. This process is known as the MeilaShi algorithm [30]. It is supported by

graph theory and is designed to extract the strongest relationships within the graph defined by the similarity matrix *S* and thus the column-wise parameters of the datasheet *M*. Note that the base 2 logarithmic used in the very definition of Q helps create a more spread-out clustering picture.

This method can help find *hidden patterns, relationships* in so many applications: disambiguate people, institutes, objects... The resulting 2D picture is shown in Figure 1. Each point of the 2D plot represents one of some 40 parameters. Each parameter representing an column of the datasheet *M* is now reduced to a 2D point. Parameters of interest are color coded. Note that the closest any two points are to each other, the closer their relationship and the further away they are from each other, the less they are correlated. The outcome reflects the findings made by the chi-square analysis. The ACR is found to be an outlier with respect to the bulk of the data parameters. The 'sex' parameter is found to be relatively central in proximity of HbA1C and 'ethnicity'. Ankle brachial index (ABI) and 'Fundoscopy Findings' are close to each other and part of what looks a sub-cluster in proximity to 'sex'.

As we can see, the resulting clustering picture allows us to develop representative focal points for the identification of potential links that would be laborious if not impossible through conventional statistical analysis. This method relies on matrix algebra and packages like MATLAB or even Python code can readily and rapidly process the basic algebra operations.