









# The relationship of climate and diabetes mellitus prevalence with applying spatial analysis; An Ecological study

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## Abstract

**Objectives:** The aims of this study were investigating the association between DM prevalence and climate conditions and finding probable hot-spot areas.

**Methods:** This ecological study conducted on disease surveillance system of DM data from rural area of two Kashan and Aran-O-Bidgol counties. It is an observational study on the disease surveillance data of health registry system including population characteristics, screened DM cases in 2016. Moran's I and Getis-Ord's index were applied to explore the hot-spot areas, and the spatial regression model were conducted for finding the relationship between climate and DM prevalence whilst adjusting some confounders, using GIS software.

**Results:** The information of 48 cities and villages with 26,800 of  $\geq 30$  years people located in three mountainous, plain and dry-desert climates were analyzed. The crude DM prevalence ranged 0-45.4%. The analysis revealed evident hot-spot areas and inverse relationship between altitude and DM prevalence ( $P < 0.05$ ).

**Conclusion:** Residences of dry-desert climate had high DM prevalence and there was a significant inverse relationship between altitude and DM prevalence.

**Keywords:** Diabetes Mellitus, Prevalence, Hot-Spot, Climate, Spatial Regression.

## Introduction

World Health Organization (WHO) has announced the diabetes prevalence as a latent pandemic in 21<sup>th</sup> century. According to a worldwide review study on more than 700 studies, the age-standardized prevalence of diabetes estimated to increase from 4.3% (2.4-7) to 9% (7.2-11.1) in men and 5.0% (2.9-7.9) to 7.9 (6.4-9.7) in women from 1980 to 2014 worldwide.<sup>[1]</sup> An estimation has predicted the number of diabetic people will rise from 285 million in 2010 to 439 million in 2030 worldwide (rising by 54%). Moreover the south Asia, the Middle east would be the hot-spot area of this disease.<sup>[2]</sup> A national survey in Iran reported 35.1% rising of diabetes prevalence in 2005-

2011.<sup>[3]</sup> While this increasing prevalence has been continued respect to the latest national survey in Iran, STEPS, in 2016, which showed the prevalence of diabetes was 9.6% in total country.<sup>[4]</sup>

In order to provide treatment and care services for diabetic patients it is required to understand the geographic distribution of DM. In addition, the geographic distributions may indicate some etiologic keys to the policy makers and health professionals. That could be achieved by depicting maps, as a useful visualized instrument. Compared to Statistics, the maps make researchers postulate novel ideas, opinions and hypothesis which could not be obtained by Statistics alone.<sup>[5]</sup>

In this regard, there has been conducted some studies which displayed geographic distribution of disease and relevance factors. For instance, in Bangladesh there was geographical differences in diabetes prevalence while adjusting demographic and socio-economic factors.<sup>[6]</sup> In another study in China, at the province level and after adjusting confounder variables, the prevalence ranged 8.3% (7.2- 9.7) in the northeast to 12.7% (11.1- 14.6) in the north of country.<sup>[7]</sup> Cunningham *et al.*, in a nationwide study in USA found standardized incidence of 310 to 2,190 (new cases /100,000) which out of 42% variant attributed to socio-economic and health-related factors.<sup>[8]</sup> In a study in USA demographic and life style factors, like physical activity, were recognized as the explanation of this diversity.<sup>[9]</sup> In order to explain the clusters of disease the socio-economic and demographic variables, as the main established risk factors of disease, have investigated as the explanation of geographic variation.<sup>[6-11]</sup>

Other than well-established risk factors of DM there are some other geographical factors which have not studied well. As a supporting evidence, in a world-wide ecologic study on type I diabetes with using 77 national indicators from 194 WHO's members, the global variations of this disease have been attributed to both geographical and demographic factors as following; climate and environment (35%), demography (33%), economy (45%) and health condition (46%).<sup>[12]</sup>

Therefore, it is necessary to other than usual risk factors some other geographical index to be investigated. In some studies elevation, average sunshine hours and altitude have been explored.<sup>[10,13,14]</sup> In a study the incidence rate of gestational diabetes at two moderate and high altitudes have compared<sup>[15]</sup> or the results of a systematic review suggested the relationship between the gestational diabetes and ambient.<sup>[16]</sup>

## Objectives

Some previous studies have suggested further research on the geographical factors of diabetes, therefore in this study the relationship between climate and DM has been explored in Kashan and Aran-o-Bidgol counties.

## Methods

This is an ecological study in the rural area of Kashan and Aran-O-Bidgol counties where are under supervision of Kashan University of Medical Sciences (KAUMS). The study area included villages and towns with cold and mountainous, plain and dry-desert climates where are distributed at various altitudes in the north of Esfahan

province with more than 15,000 Km<sup>2</sup> area and 36,759 ≥30 people.

The analysis conducted on the data of DM health care program. As a part of Iran's ministry of health and medical education (MOME) health programs. All residents ≥30 of villages and towns less than 50,000 are screened for diabetes and hypertension in a five-year period with fasting blood sugar test (FBS) and mercury sphygmomanometer. According to pre-determined cut off, people with FBS less than 100, 100-125 and ≥126 mg/dl are considered as healthy, pre-diabetic and diabetic, accordingly. The diagnosed cases will follow for more health care services. In this study, the latest results of mass screening in 2016 were used. These data included the population size of people ≥30 and screened people under supervision of every health unit (House of Health - Khaneh Behdasht-and Health Base). The altitude of area was captured from Kashan municipality which has been obtained from web-based software of google earth.

For analysis, in order to specify the clusters of disease as the hot-spots, the spatial autocorrelation was checked using Moran's I and Getis-Ord's index.<sup>[5]</sup> Furthermore, the relationship between altitude and diabetes prevalence explored through spatial regression model, adjusting for the participation of people in screening program, as the proxy of people's self-care.

In order to control two confounding factors of age and sex, instead of the crude prevalence, age and sex-standardized prevalence ratio (ASPR) was applied in spatial model as the dependent variable. For independent factors, DM screened ratio (DMSR), and altitude (in meter from free sea level) were used in model.

In order to calculate ASPR, Indirect method of standardization was applied which the total population of county was applied as the reference population, using Excel software.

It is notable, because of sample size issue, the altitudes of areas were used in spatial regression model, instead of categorized climate variable.

## Ethical considerations

The study was conducted in accordance with the Declaration of Helsinki. This study was approved by ethical board of KAUMS with code IR.KAUMS.MEDNT.REC.1397.109. All participants signed an informed consent form.

## Results

This study was conducted in 2019. In summary, data of

48 villages and towns were used. The average participation proportion in screen program was 44.5% (ranged 6-100%) which were 35% and 54% for males and females. The lowest proportion was about Josheghan-e-Ghali and Alavi and the highest one was about Eznaveh. The crude DM prevalence was 11.2%, which for males and females were 8.6% and 12.9% respectively.

To the point of place-specific prevalence, there were considerable variabilities among studied places. The highest prevalence belonged to Kaghazi village with 45.4% and the lowest one was for Chogan with 0%. More details are in attachment 1.

To investigate the spatial autocorrelation, Moran's I and Getis-Ord's index were used [5,17]. The Getis-Ord Gi-Star showed diverse ASPR ranged 0.11-3.80. There were hot-spot clusters with high prevalence of DM at the east regions of KAUMS's area, which are located on dry desert

climate. The map shows by moving from mountainous to dry desert area the ASPR rises gradually [Figure 1].

Other than Getis-Ord's index, Moran's I index obtained. The obtained statistic was 0.06 which is obviously different from expected value as the pre-required value for independency of area's ASPR. It is near to significant level (P=0.07) with positive Z-score. The positive sign of Z-score implies clusters of areas with high SPR [18-19] [Figure 2].

The spatial regression model revealed inverse significant relationship between the altitude and ASPR adjusting for DMSR (P<0.05). In other words, by increasing the altitudes' height the ASPR declines. There was also positive relationship between DMSR and ASPR which implies by increasing the screening ratio, ASPR increases (P<0.05). The index of model was as follow; adjusted R<sup>2</sup> 0.41, AIC 61.51 and VIF 1.20 [Table 1].

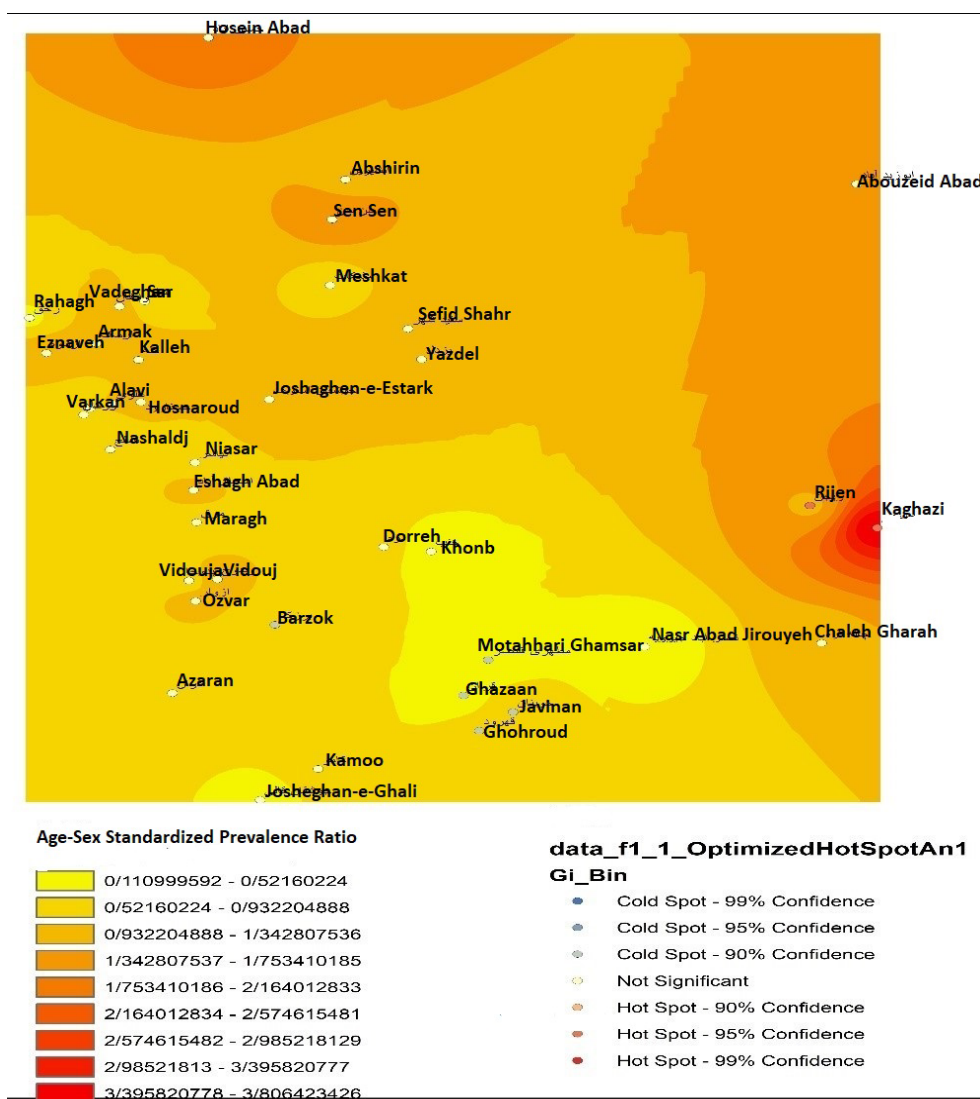
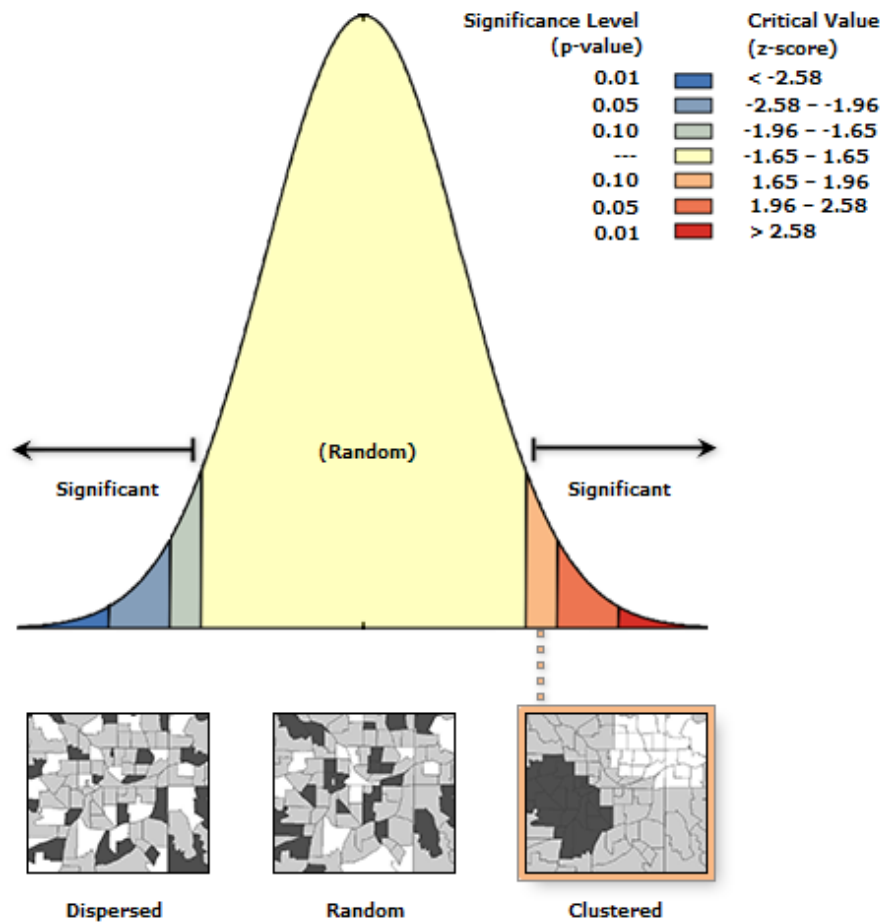


Figure 1. The ASPR distribution of DM in studied areas



**Figure 2.** The probability distribution of ASPR under the hypothesis of random dispersion

**Table 1.** The summary of applied spatial regression model

Model statistics						Model
AdjR2	AICc	JB	K(BP)	VIF	SA	
0.41	61.51	0.00	0.25	1.20	0.60	+SELF_CARE* -HEIGHT*

AdjR2; Adjusted R-Squared, AICc; Akaike's Information Criterion, JB; Jarque-Bera p-value, K(BP); Koenker (BP) Statistic p-value, VIF; Max Variance Inflation Factor, SA; Global Moran's I p-value, Model Variable sign (+/-), Model Variable significance (\*= 0.01).

## Discussion

This study showed DM's clusters in studied areas obviously. In addition, there was a significant inverse relationship between climate and DM prevalence, adjusting for age, sex and self-care variables. Regarding dry-desert areas have low altitudes and the mountainous one has high altitudes, there is a relationship between climate and DM in which the dry-desert areas have higher DM prevalence than the mountainous ones.

There are some supporting evidences for this finding. In an ecological study on type I diabetes at the international scale using 77 national indicators of 80 countries, a main part of between countries variance belonged to climate and environment (35%) whilst for demography, economy and health condition they were 33%, 44% and 46% of total

variance.<sup>[12]</sup> That study showed contributing role of climate on DM. At the national level, in another cross-sectional study in USA, adjusting demographic, socio-economic, ethnicity, life-style and diet variables, there was inverse relationship between altitude and DM in adult men, but not in women.<sup>[14]</sup>

From the physiological standpoint, there are some supporting evidences. according to a review study by Woolcott et al., the residences of high altitudes (over 1500 m) had lower fasting glycemia, obesity and DM prevalence.<sup>[20]</sup> In another national level study in Peru, DM prevalence in coastal and jungle areas were higher than high altitude ones.<sup>[21]</sup> In contrast, in a national-level cohort study in Peru, the incidence of DM in high altitude was about two times of low altitude areas which shows

requiring more studies.<sup>[13]</sup>

To explain the reason of this relationship, some hypothesis has been proposed. As the earliest, James Neel introduced “thrifty gene hypothesis”.<sup>[22]</sup> According to this hypothesis the ancestors of people with hot-climate origin had been suffered from sequential famines which caused many deaths; those who survived had metabolic abilities which consumed low intake calories more efficiently. The people without this ability did not survive. Since in recent century there is enough or even more food intake so the intake calories are over than the body needs in people carrying “thrifty gene” which induces DM. Since the inhabitants of hot land area compared to cold areas have more experience of famines in last centuries, therefore the thrifty gene are more prevalent in these areas. However, later Neel rejected his hypothesis due to lack of enough evidences.<sup>[23]</sup> In spite of rejecting this hypothesis by his author, there is supporting evidence which shows the relationship between famine and DM development. As a historical and natural experiment in the Netherlands, the children born from the women who experienced famine during late gestational period, in 1944-45, had more glucose intolerance, increased insulin resistance and DM in adulthood.<sup>[24]</sup>

Fridlyand and et al., proposed other hypothesis for this issue, named “cold climate genes”. This was proposed to explain the higher DM prevalence among the immigrants of hot-origin area compared to European origins.

This hypothesis assumes cold climate stops some metabolic pathways leading to DM. The ancestors of cold climate regions had to adopt available seasonal food and calorie changes, moreover when they immigrated to higher latitudes with colder conditions, such as European countries, they had to adapt to colder climate. This condition demand a set of genes which not only suppressing unnecessary physiological mechanism in previous hotter zones, but also adopting to cold climate which they immigrated.<sup>[25]</sup>

These two hypotheses have been proposed as the explanations of higher DM either in hot zone areas or low altitude areas which in both of them gene plays the main role. In order to verify this hypothesis, at the first step, it had better to establish having any differences in DM risk among different climates then seek those gene which may are responsible for that.

This study had a number of strengths. Firstly, the effect of age and sex were adjusted. Secondly, by studying on a limited area it is expected to have homogenous study population in terms of ethnicity, life styles and health services as some possible factors for explanations whilst

having different climates in this restricted area. This property of study provided the study opportunity for distinction between climate effect and other factors although such data for verifying the homogeneity of those variable were not available.

This study had some limitations; using screening ratio as the proxy of life style was one of them. Due to lack of data, the screen ratio indicator applied instead. Considering the probable effect of climate through genes in one side and close social relationship between the studied areas on the other side, genetic mixing may be happened by marriages over ages. It is happened in particular in adjacent cities and villages which resulted in mixing genes. This is really a probable obstacle for applying gene hypothesis as the explanation of heterogeneity of DM over studied areas in this study. Further genetic studies are required, since the familial marriage in Iranian society is more common.

In statistical point of view, despite using sophisticated statistical model the studied units were small, therefore the statistical noise might have been occurred. The small unit areas have small denominator, therefore any small changes in DM number, as the nominator, affect the prevalence values drastically which called statistical noise. To solve this problem, we should use smoothed data in this case. However, having a range of 45% differences and evident pattern in DM distributions, attributing such findings to this problem is not advisable.

As the further studies, to distinguish between climate, gene and life style, studying on immigrant and emigrant people in these areas may be informative. Moreover, recruiting genetic Epidemiology approach could be helpful.

## Conclusions

There was evident pattern in DM prevalence over studied areas and the significant relationship with altitudes. To approve this relationship more clearly, more detailed information about individual, genetic, social and cultural factors are required.

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## Competing interests

The authors declare that they have no competing interests.



## Abbreviations

World Health Organization: WHO;  
 Fasting blood sugar: FBS;  
 Diabetes Mellitus: DM;  
 Age and sex-standardized prevalence ratio: ASPR;  
 DM screened ratio: DMSR;  
 AdjR2: Adjusted R-Squared;  
 AICc: Akaike's Information Criterion;  
 JB: Jarque-Bera p;  
 VIF: Variance Inflation Factor.

## Authors' contributions

All authors read and approved the final manuscript. All authors take responsibility for the integrity of the data and the accuracy of the data analysis.

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## Availability of data and materials

The data used in this study are available from the corresponding author on request.

## Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki. This study was approved by ethical board of KAUMS with code IR.KAUMS.MEDNT.REC.1397.109. All participants signed an informed consent form.

## Consent for publication

By submitting this document, the authors declare their consent for the final accepted version of the manuscript to be considered for publication.

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#### Attachment 1. Crude sex specific prevalence in studied areas

Num	Place name	Climate	≥30 years old			Screened ratio (%)			Prevalence ratio (%)		
			Men	Women	Total	Men	Women	Total	Men	Women	Total
1	Eznaveh	Mountainous	53	74	127	100.0	100.0	100.0	9.4	20.3	15.7
2	Geh	Mountainous	20	32	52	N/D	N/D	N/D	N/D	N/D	N/D
3	Armak	Mountainous	112	118	230	100.0	100.0	100.0	6.3	12.7	9.6
4	Vadeghan	Mountainous	111	133	244	91.9	97.7	95.1	4.9	23.1	15.1
5	Rahagh	Mountainous	165	172	337	99.4	91.9	95.5	1.8	6.3	4.0
6	Sar	Mountainous	27	37	64	100.0	97.3	98.4	11.1	22.2	17.5
7	Kalleh	Mountainous	77	117	194	100.0	100.0	100.0	11.7	17.1	14.9
8	Sen Sen	Plain	660	599	1259	47.0	62.1	54.2	0.6	1.1	0.9
9	Abshirin	Plain	N/D	N/D	N/D	N/D	N/D	N/D	N/D	N/D	N/D
10	Meshkat	Plain	1137	1119	2256	14.1	32.2	23.0	2.5	3.9	3.5
11	Kamou	Mountainous	N/D	N/D	N/D	N/D	N/D	N/D	15.1	20.7	17.8
12	Chogan	Mountainous	N/D	N/D	N/D	N/D	N/D	N/D	0.0	0.0	0.0
13	Gosheghan-e-Ghali	Mountainous	856	983	1839	10.5	2.8	6.4	3.3	3.6	3.4
14	Azeran	Mountainous	249	279	528	22.5	28.0	25.4	14.3	7.7	10.4
15	Vidouj	Plain	264	316	580	92.0	97.2	94.8	6.2	7.8	7.1
16	Vidouja	Plain	234	259	493	91.9	93.8	92.9	2.8	8.6	5.9
17	Ozvar	Mountainous	173	200	373	69.4	85.0	77.7	7.5	11.2	9.7
18	Tajareh	Mountainous	73	86	159	90.4	46.5	66.7	3.0	5.0	3.8
19	Pendas	Mountainous	76	86	162	35.5	46.5	41.4	0.0	5.0	3.0
20	Varkan	Mountainous	153	179	332	64.7	58.7	61.4	1.0	4.8	2.9
21	Barzok	Mountainous	N/D	N/D	N/D	N/D	N/D	N/D	N/D	N/D	N/D
22	Sadian	Mountainous	N/D	N/D	N/D	N/D	N/D	N/D	N/D	N/D	N/D
23	Maragh	Mountainous	366	303	669	44.8	80.2	60.8	7.9	13.2	11.1
24	Estark	Mountainous	349	375	724	33.8	57.3	46.0	14.4	11.6	12.6
25	Fath Abad	Mountainous	N/D	N/D	N/D	N/D	N/D	N/D	N/D	N/D	N/D
26	Josheghan-e-Estark	Plain	483	447	930	9.3	24.8	16.8	11.1	13.5	12.8
27	Alavi	Mountainous	180	199	379	2.8	10.1	6.6	60.0	25.0	32.0

28	<b>Bari Karafs</b>	Mountainous	80	97	177	76.3	85.6	81.4	8.2	8.4	8.3
29	<b>Nashaldge</b>	Mountainous	519	541	1060	83.8	88.9	86.4	4.1	14.1	9.4
30	<b>Hosnaroud</b>	Mountainous	166	167	333	68.7	77.8	73.3	6.1	10.8	8.6
31	<b>Javinan</b>	Mountainous	N/D	N/D	N/D	N/D	N/D	N/D	N/D	N/D	N/D
32	<b>Ghohroud</b>	Mountainous	299	231	530	54.8	89.2	69.8	9.1	18.9	14.6
33	<b>Khonb</b>	Mountainous	160	155	315	82.5	91.6	87.0	5.3	11.3	8.4
34	<b>Dorreh</b>	Mountainous	N/D	N/D	N/D	N/D	N/D	N/D	N/D	N/D	N/D
35	<b>Ghazaan</b>	Mountainous	49	67	116	61.2	62.7	62.1	3.3	4.8	4.2
36	<b>Ghamsar 1**</b>	Mountainous	N/D	N/D	N/D	N/D	N/D	N/D	N/D	N/D	N/D
37	<b>Ghamsar 2</b>	Mountainous	N/D	N/D	N/D	N/D	N/D	N/D	N/D	N/D	N/D
38	<b>Eshagh Abad</b>	Mountainous	71	93	164	84.5	96.8	91.5	5.0	11.1	8.7
39	<b>Niasar</b>	Mountainous	228	250	478	81.1	95.2	88.5	28.1	29.8	29.1
40	<b>Chaleh Gharah</b>	Plain	N/D	N/D	N/D	N/D	N/D	N/D	N/D	N/D	N/D
41	<b>Nasrabad Jirouyeh</b>	Plain	N/D	N/D	N/D	N/D	N/D	N/D	N/D	N/D	N/D
42	<b>Abouzeidabad</b>	dry-desert	1442	1292	2734	8.5	40.6	23.6	11.5	16.6	15.6
43	<b>Kaghazi</b>	dry-desert	403	351	754	24.8	45.6	34.5	41.0	48.1	45.4
44	<b>Aliabad-e-Fakhreh</b>	dry-desert	281	260	541	39.5	36.5	38.1	5.4	5.3	5.3
45	<b>Rijen</b>	dry-desert	176	156	332	9.1	53.2	29.8	0.0	8.4	7.1
46	<b>Mohammad Abad</b>	dry-desert	468	500	968	15.4	49.8	33.2	16.7	12.4	13.4
47	<b>Ghasem Abad</b>	dry-desert	213	214	427	53.5	98.1	75.9	12.3	18.6	16.4
48	<b>Hosein Abad</b>	dry-desert	435	419	854	5.5	24.8	15.0	16.7	7.7	9.4
49	<b>Sefid Shahr</b>	Plain	1225	1070	2295	12.8	38.2	24.7	12.1	13.0	12.7
50	<b>Yazdel</b>	Plain	631	593	1224	25.5	55.6	40.1	9.9	4.2	6.1
51	<b>Mohammad Abad-e-Kavir</b>	dry-desert	507	458	965	21.5	68.1	43.6	22.0	15.7	17.3
52	<b>Ali Abad-e-Kavir</b>	dry-desert	297	305	602	42.4	85.9	64.5	7.1	16.4	13.4
	<b>Total</b>		13468	13332	26800	34.6	54.4	44.4	8.6	12.9	11.2

\*N/D denotes No Data

\*\*Ghamsar city has two urban health centres