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Original Article

Coprevalence of parasitic infections and diabetes in Sub-Himalayan region of Northern India

Vaishali Moudgil[1], Reetima Rana[1], Praveen Kumar Tripathi[2], Umar Farooq[1], Rakesh Sehgal[2], Mohammed Azhar Khan[1]

[1]Department of Biotechnology, School of Biotechnology, Shoolini University of Biotechnology and Management Sciences, Solan, Himachal Pradesh, India, [2]Department of Parasitology, Post Graduate Institute of Medical Education Research, Chandigarh, Punjab, India

Address for correspondence:
Dr. Mohd Azhar Khan, Faculty of Biotechnology, Shoolini University of Biotechnology and Management Sciences, Post Box No. 9, Head Post Office, Solan - 173 212, Himachal Pradesh, India. E-mail: mk.azhar1@gmail.com

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ABSTRACT

Objectives: Parasitic infections such as toxoplasmosis, hydatidosis, and cysticercosis infect a large population worldwide. *Toxoplasma gondii* in the pancreas could damage the pancreatic cells. Hence, insulin secretion would be affected which leads to increased risk of diabetes. The present study was designed to investigate the cooccurrence of parasitic infections in patients with diabetes.

Methods: A total of 256 confirmed parasitic serum samples were included in the study, of which 95 were positive for toxoplasmosis, 87 for hydatidosis, and 74 for cysticercosis infection. These samples were then analyzed for hyperglycemia.

Results: In case of hydatidosis, the frequency of hyperglycemia was 14.94%, followed by cysticercosis (10.8%) and toxoplasmosis (8.42%). The frequency of insulin resistance was analyzed in these hyperglycemic samples. The coprevalence of diabetes was higher in case of hyperglycemic hydatidosis patient samples (11.49%), followed by cysticercosis (8.10%) while the coprevalence of diabetes was minimum (6.31%) in toxoplasmosis patients samples. Thus, the overall prevalence of diabetes with parasitic infections was 8.6%.

Conclusion: The study suggested the coexistence of hyperglycemia in hydatidosis, cysticercosis, and toxoplasmosis infected samples. However, higher prevalence of high glucose level was detected among hydatidosis infected samples. Thus, suggested individuals infected with hydatidosis were more susceptible for diabetes in comparison to toxoplasmosis and cysticercosis.

Keywords: Cysticercosis, diabetes, hydatidosis, parasitic infections, toxoplasmosis

Introduction

Diabetes mellitus (DM) is one of the common non-communicable diseases caused by deficiency or diminished effectiveness of endogenous insulin either because insulin production is inadequate, or the body's cells do not respond properly to insulin or both.[1] A parasitic disease is an infectious disease caused by a parasite. Many parasites do not cause overt diseases; however, some can infect all living organisms including plants and mammals. Parasitic diseases have been consistently reported in association with diabetic patients.[2] Intestinal parasites usually produce benign diseases but may cause complications with high mortality and morbidity.[3,4] It is known that the diabetic patients are more susceptible to bacterial infections. Decreased arterial perfusion, neuropathy, and suppressed immune response in diabetes aggravate the frequency and severity of infectious diseases.[5]

It has also been reported that candidal infections occur more frequently in diabetic patients than in non-diabetic individuals.[6,7] The elderly persons more susceptible to severe ocular *Toxoplasma* infections due to age-related decline in cell-mediated immunity and chronic underlying diseases.[8] Parasitic diseases have been reported in association with diabetic patients. However, it is not clear whether parasitic infections can increase the risk of diabetes or diabetes can lead to an increased risk of parasitic infections. These include amoebiasis, cryptosporidiosis, cutaneous leishmaniasis, strongyloidiasis, and hydatid cyst.[9-13] Several case reports have also shown the presence of hydatidosis and cysticercosis in diabetic patients.[13,14]

Thus, in view of the available information, the present study was designed to analyze the hyperglycemic, seropositive samples from *Toxoplasma gondii*, *Echinococcus granulosus,* and *Taenia solium* infected patients and to investigate their correlation or coprevalence of diabetes in sub-Himalayan region of Northern India.

Methods

Samples

The serum samples were obtained from Molecular and Immuno-Parasitology Research Laboratory, Shoolini University, Solan, and Department of Medical Parasitology, PGIMER, Chandigarh. A total of 256 samples were included in the study, which were seropositive for toxoplasmosis, cysticercosis, and hydatidosis. Of 256 serum samples, 95 were positive for toxoplasmosis, 87 for hydatidosis, and 74 for cysticercosis. The study protocol has been approved by the Institutional Ethical Committee (IEC) of Shoolini University, wide letter no. SUBMS/IEC/11/45-46. Written informed consent was taken from all participants.

Blood glucose level estimation

The blood glucose level in serum samples was determined using commercially available kits according to the manufacturer's instruction: Blood glucose concentration in serum was measured enzymatically with the help of a commercial kit (Autozyme Glucose STAT) according to the manufacturer's instructions.

Measurement of insulin level to determine insulin sensitivity

The insulin level in serum was measured to determine the level of insulin using commercially available insulin ELISA kit (DRG Insulin ELISA) according to the manufacturer's instruction.

Calculation of homeostasis model assessment insulin resistance (HOMA IR)

For the reconfirmation of IR, HOMA-IR was calculated by applying the following formula:

$$\text{HOMA IR} = \frac{\text{Glucose } (\text{mg/dl}) \times \text{Insulin } (\text{mg/dl})}{405}$$

Statistical Analysis

Statistical analysis was carried out using the GraphPad Prism software. The methods for statistical analysis included in this study were Student's *t*-test and one-way ANOVA (if $P \leq 0.05$ = significant and if $P \geq 0.05$ = Non-significant).

Results

Frequency of hyperglycemia in toxoplasmosis-positive samples

Of 95 serum samples positive for *Toxoplasmosis,* 34.7% (33/95) were from male patients and 65.26% (62/95) were from females. The frequency of hyperglycemia in *Toxoplasma*-positive samples was analyzed and was found to be 8.42% (8/95) in the overall population [Table 1]. The frequency of hyperglycemic condition was 12.12% (4/33) in males and 6.45% (4/62) in females. Thus, males were more susceptible to hyperglycemia as compared to females (here, *P* value is non-significant, but the data suggest that hyperglycemia in males is on a higher side. This can be due to low sample size) [Figure 1].

Frequency of Hyperglycemia in Hydatidosis-Positive Samples

Of 87 hydatidosis-positive serum samples, 49.4% (43/87) were from males and 50.57% (44/87) were from female patients. The frequency of hyperglycemia in hydatidosis samples was analyzed and it was found that 14.94% (13/87) of the patients with hydatidosis was hyperglycemic [Table 2]. The frequency of hyperglycemic condition in males was 11.62% (5/43) while in females, it was 18.18% (8/44). Hence, females were more susceptible for hyperglycemia as compared to males (*P* value non-significant, but the data suggest that hyperglycemia in females with hydatidosis is on a higher side. This can be due to low sample size) [Figure 2].

Frequency of hyperglycemia in cysticercosis-positive samples

Of 74 cysticercosis samples, 52.7% (39/74) were male and 47.2% (35/74) were female. The frequency of hyperglycemia in cysticercosis samples was analyzed, and it was found that 10.8% (8/74) of the patients with cysticercosis were hyperglycemic [Table 3]. The frequency of hyperglycemic condition in males was 12.82% (5/39) while in females, it was 8.75% (3/35). The results indicate that males were

Table 1: Frequency of hyperglycemia among toxoplasma seropositive males and females (*n*=95)

Sex	Normal	Hyperglycemic	Total
Male	29	4	33
Female	58	4	62
Total	87	8	95

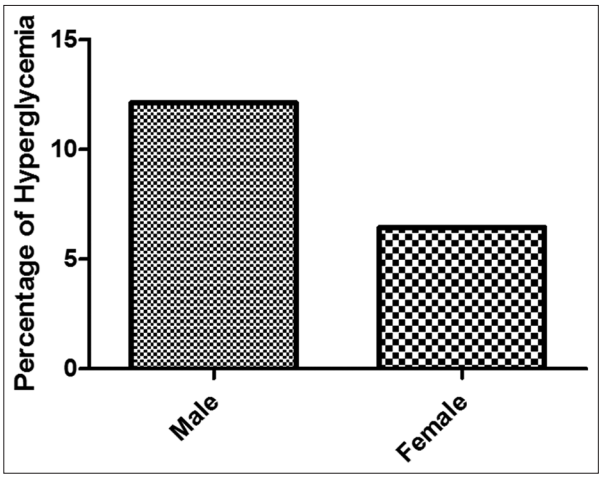

Figure 1: Frequency of hyperglycemia in toxoplasmosis-positive males and females

Table 2: Frequency of hyperglycemia among males and females hydatidosis samples (*n*=87)

Sex	Normal	Hyperglycemic	Total
Male	38	5	43
Female	36	8	44
Total	74	13	87

Table 3: Frequency of hyperglycemia among male and female cysticercosis samples (*n*=74)

Sex	Normal	Hyperglycemic	Total
Male	34	5	39
Female	32	3	35
Total	66	8	74

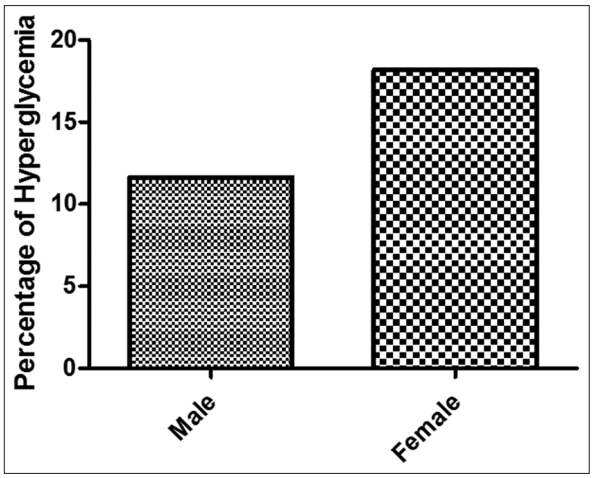

Figure 2: Frequency of hyperglycemia in males and female hydatidosis-positive samples

more susceptible for hyperglycemia as compared to females (here, *P*-value is non-significant, but the data suggest that hyperglycemia in males with cysticercosis is on a higher side. This can be due to low sample size) [Figure 3].

Determination of insulin level in hyperglycemic toxoplasmosis, hydatidosis, and cysticercosis samples

The insulin levels were determined among hyperglycemic toxoplasmosis-, hydatidosis-, and cysticercosis-positive samples. It was found that the insulin level in case of hyperglycemic hydatidosis was 40 µlU/ml, and in hyperglycemic cysticercosis and toxoplasmosis samples, the insulin level was 35 µlU/ml. A significant difference in insulin level was observed when the serum samples from normal individuals (non-hyperglycemic) were compared with those from hyperglycemic toxoplasmosis, hydatidosis, and cysticercosis patients ($P \leq 0.001$) [Figure 4].

Frequency of IR in hyperglycemic parasite-infected samples

The frequency of IR was found to be highest in hyperglycemic hydatidosis patients' serum samples (77%) followed by

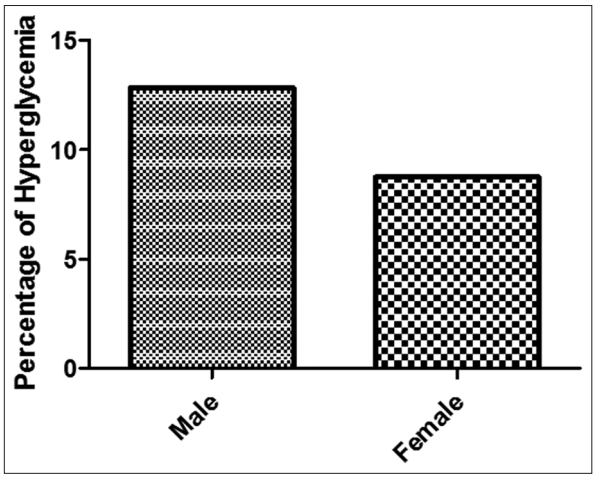

Figure 3: Frequency of hyperglycemia in males and female cysticercosis-positive samples

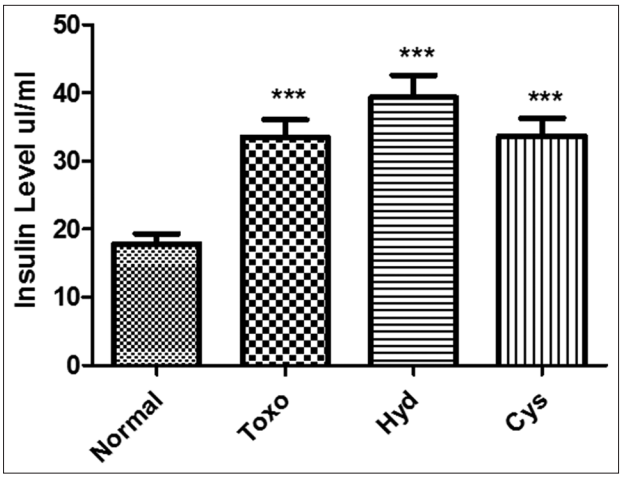

Figure 4: Insulin level in normal condition and hyperglycemic parasite-infected condition. Toxo: Toxoplasmosis, Hyd: Hydatidosis, Cys: Cysticercosis

cysticercosis (75%) and toxoplasmosis (75%) patients' serum samples. However, the other hyperglycemic samples were not considered to be IR as they fell within the range of borderline, that is, 25 µlU/ml [Table 4].

Calculation of HOMA IR

The IR was confirmed by HOMA IR:

$$\text{HOMA IR} = \frac{\text{Glucose } (\text{mg/dl}) \times \text{Insulin } (\text{mg/dl})}{405}$$

As expected, the HOMA IR results were found similar to the results of IR in hyperglycemic parasite-infected samples. The frequency of HOMA IR percentage was highest in hydatidosis samples (23%), followed by toxoplasmosis and cysticercosis samples where the frequency of HOMA IR percentage was 19% (No significant difference was found among the three populations) [Figure 5].

Prevalence of Diabetes with toxoplasmosis, hydatidosis, and cysticercosis patients' samples

Of 95 toxoplasmosis samples, 6.31% (6/95) of the samples were found to be IR. In case of 87 hydatidosis samples, only 11.49% (10/87) of the samples were IR, whereas of 74 cysticercosis samples, 8.10% (6/74) of the samples were IR. Thus, the overall prevalence of diabetes was highest with hydatidosis followed by cysticercosis and toxoplasmosis [Figure 6].

Overall prevalence of diabetes with parasitic infected samples

Of 256 parasitic infected samples, the overall prevalence of hyperglycemia was 11.3% (29/256), and of these hyperglycemic samples, only 8.6% (22/256) were found to be IR [Figure 7].

Discussion

DM is a major and growing health problem in most countries and an important cause of prolonged ill health and early death.[14,15] Its prevalence is increasing all over the world due to population growth, aging, urbanization, and an increase in obesity, physical inactivity, and various other factors including environmental triggers.[16-21] Diabetes in Asian countries is disproportionately high in young to middle-aged adults.[22] Globally, it is estimated that 382 million people suffer from diabetes which accounts for an overall prevalence of about 8.3%.[23]

Table 4: IR in hyperglycemic parasitic infected samples

Insulin Status	Toxoplasmosis samples	Hydatidosis samples	Cysticercosis samples
Hyperglycemic	8	13	8
IR	6 (75%)	10 (77%)	6 (75%)

IR: Insulin resistance

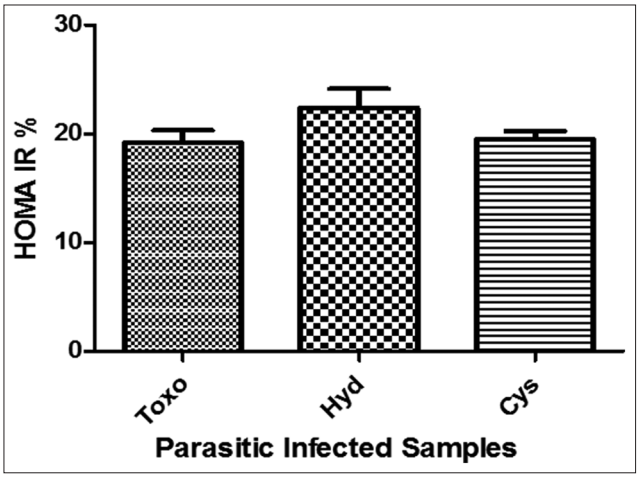

Figure 5: Determination of homeostasis model assessment insulin resistance percentage in hyperglycemic parasitic infected samples. Toxo: Toxoplasmosis, Hyd: Hydatidosis, Cys: Cysticercosis

Intestinal parasitic infections are globally endemic and have been described as major cause of illness and disease worldwide. Poverty, illiteracy, poor hygiene, lack of access to potable water, and hot and humid tropical climate are the factors associated with intestinal parasitic infections.[24] It is estimated that some 3.5 billion people are affected, and 450 million are ill as a result of these parasitic infections the majority being children. Apart from considerable morbidity and mortality, the parasitic infections are known to cause anemia, growth retardation, and other physical and mental health problems.[25]

The individuals suffering from DM become immune compromised and prone to parasitic infections.[26,27] Intestinal parasites have gained attention as important opportunistic pathogens responsible for clinically important infections in immune-compromised patients.[26,27] In the present study, the results showed that DM condition has a significant risk factor for acquiring parasitic infections. However, this differs from the findings of Nazligul *et al*.[28] report where non-DM individuals had a significantly higher prevalence of intestinal parasitic infections.

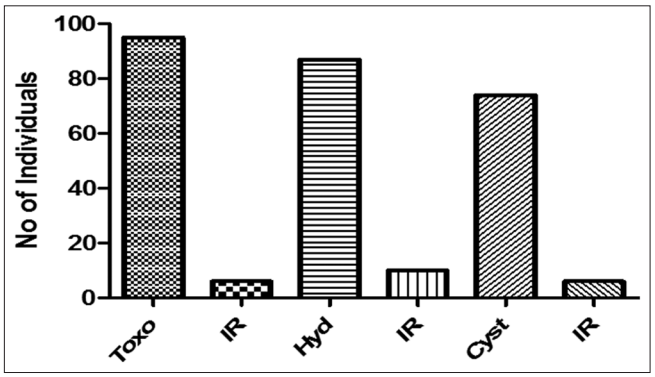

Figure 6: Bar diagram showing the prevalence of diabetes (IR) with toxoplasmosis-, hydatidosis-, and cysticercosis-positive samples. Toxo: Toxoplasmosis, Hyd: Hydatidosis, Cyst: Cysticercosis, IR: Insulin resistance

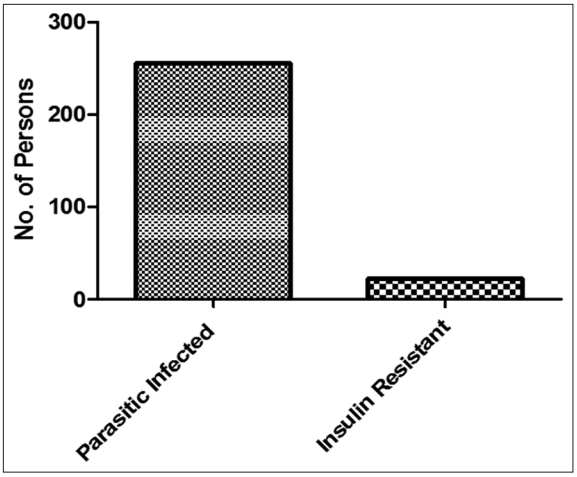

Figure 7: Prevalence of diabetes with parasitic infected sample

The present study was conducted to detect the diabetic condition in patients having parasitic infections: Toxoplasmosis and cysticercosis. In this study, 256 serum samples from seropositive patients were analyzed. The overall prevalence of diabetes with parasitic infection was observed to be 8.6%. A similar study conducted by Akinbo *et al*.[29] concluded that the overall prevalence of intestinal parasitic infection among DM patients was 18.7% which is higher in comparison to our study, and no case of parasitic infection was reported among the non-DM individuals. However, the study conducted by Akinbo *et al*. was based on the prevalence of intestinal parasitic infections where *Ascaris lumbricoides, Entamoeba histolytica*, and hookworm, that is, only the intestinal parasites were studied in DM patients, whereas in our study, *T. gondii*, *Echinococcus granulosus*, and *T. Solium,* that is, the non-intestinal parasites were linked with DM.

In our study, of 256 serum samples, 95 were from ELISA confirmed toxoplasmosis patients. The prevalence of diabetes in these samples was observed to be 6.31%. A similar case study conducted in Iran reported the 2-fold higher prevalence of DM in toxoplasmosis patients in comparison to the healthy individuals.[30] Interestingly, Nissaptor *et al*.[31] reported a 61.1% prevalence of toxoplasmosis in diabetic patients which is almost 8-fold higher in comparison to our study. Similarly, in a case report, Mohamed *et al*.[32] showed that a female infant suffering from diabetes was also found positive for toxoplasmosis.

A total of 87 samples were found to be positive for hydatidosis infection. The prevalence of diabetes in these samples was observed to be 11.49%. A similar study by Florea *et al*.[33] reported a hydatid liver cyst in diabetic patients. However, in this study, the prevalence of diabetes in hydatidosis was less as compared to our finding.

The prevalence of diabetes among 74 cysticercosis confirmed samples was observed to be 8.10%. Similar to this study, Yang *et al*.[13] reported neurocysticercosis (NCC) in diabetic children. However, such a study of NCC was the first report of its kind. Here, the prevalence of diabetes in cysticercosis was very less as compared to our study.

In our study, toxoplasmosis- and cysticercosis-positive males were found to be more susceptible to hyperglycemia as compared to females, whereas hydatidosis-positive females were found to be more susceptible to hyperglycemia as compared to hydatidosis-positive males. However, Akinbo *et al*.[29] reported that the gender was not a risk factor for acquiring intestinal parasites in DM patients.

Conclusion

The present study analyzed the hyperglycemic, seropositivity of toxoplasmosis, hydatidosis, and cysticercosis in patients with diabetes, which may be important for developing the strategies to prevent/cure the prevalence of parasitic infections in diabetes patients.

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