Enteric Parasites in Patients with Diarrhoea Presenting to a Tertiary Care Hospital: Comparison of Human Immunodeficiency Virus Infected and Uninfected Individuals

Sir,

In resource limited countries such as India, parasitic enteric infections remain common in the general population and in the HIV infected, with geographic differences in the reported prevalence of individual pathogens reflecting differences in pathogen prevalence, standards of hygiene and diagnostic methods used. In this study, we report the prevalence of enteric parasites in HIV positive and HIV negative individuals with diarrhoea over a five year period from January 1998 to December 2002.

The study was conducted in the Christian Medical College, Vellore, in patients presenting to the Infectious Disease Clinic or the Gastroenterology department with a history of diarrhoea. Specimens were received from 258 HIV infected and 4103 non-infected individuals, and processed by standard methods for parasite identification. The data were entered in Excel and analysed using SPSS v.9. Fisher’s exact test was applied to determine differences in the two groups in each year. Student’s t-test was used to assess differences in proportion of infections due to each individual parasite.

Enteric parasites were identified in 57.3% of 258 samples from HIV infected individuals, with multiple pathogens identified in 6.6%. Protozoan parasites were common, with Isospora belli (19.7%), Cryptosporidium (15.5%), Giardia lamblia (5.0%) and Cyclospora cayatenensis (3.8%). Microsporidia were seen in 4.6%. The helminths identified were Strongyloides stercoralis larvae (8.5%), Ascaris lumbricoides ova (2.3%) and hookworm ova (4.3%). During the same period, 4103 samples from control patients with diarrhoea were examined. Enteric parasites were identified in 5.8% of samples. Giardia lamblia was the commonest identified pathogen, seen in 2.61%, with Isospora in 0.51%, Cryptosporidium in 0.37% and Cyclospora in 0.15%. The helminths identified were Strongyloides in 0.95%, hookworm in 0.80% and Ascaris 0.39%. Multiple parasites were not noted. The difference in identification of parasites between the two groups of HIV infected and uninfected are statistically significant in each year (Fisher’s exact test p < 0.00). The relative distribution of Isospora belli, Cryptosporidium parvum and microsporidia was significantly more prevalent in HIV infected individuals (p<0.00 for all three parasites, Student’s t-test), while the difference in proportion of infections due to Strongyloides stercoralis was not statistically significant. The overall frequency distribution of the different types of parasites among the parasitic infections was significantly different between the two groups (Chi square p<0.00).

This five year study showed that parasitic diarrhoea is 10 times more common in HIV positive patients than in HIV-negative patients (57.3% versus 5.8%, p<0.00). Protozoal pathogens that cause opportunistic infections of the gut are Cryptosporidium parvum, Isospora belli and microsporidia and these were seen in 40% of all HIV positive patients with diarrhoea. In recent years, it has been shown that HIV infection and parasitic infections interact and have a mutual deleterious effect. Parasitic infection may facilitate the progression from asymptomatic HIV infection to AIDS by a chronic immune activation, particularly with T-helper 2 type responses. Studies using surrogate markers of AIDS, like CD4 counts and HIV viral load in addition to these tests will elucidate the dynamics of infective diarrhoea in HIV patients.

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REFERENCES

Association of Small Dense LDL with a Coronary Artery Disease and Diabetes in Urban Asian Indians - The Chennai Urban Rural Epidemiology Study (CURES 8)

Sir,

As aptly pointed out by V Mohan et al, conventional techniques to measure the small, dense LDL-C are cumbersome and not easily available in clinical practice. The atherogenic plasma index (AIP) proposed by M Dobiasova and Fronhlich is a logarithmic transformation of the ratio of the molar triglyceride (TG) concentration and high density lipoprotein cholesterol (HDL-C) (log (TG/HDL-C)). AIP has been devised, based on analysis of results of 11 previous studies where
FERHDL and plasma lipid parameters were investigated in different groups of people who differed as to the atherogenic risk. The mean AIP values of non-risk groups is zero or were lower, while with an increasing atherogenic risk AIP reached positive values, including high positive values in risk groups (plasma of diabetic subjects, patients with positive angiography, myocardial infarction, etc.).

We presented our data at the Dr DP Basu Awarded Lecture, 56th Annual Conference of CSI, Kolkata, December 2003 from the study to assess association of LDL and its particles size in context with endothelial dysfunction and CAD in 367 patients. The strongest correlation of AIP was noted with triglycerides where a prevalence of small dense LDL-C was significantly higher among subjects with TG > 150 mg/dl (99.4% vs 64.7%, p < 0.0001) and in subjects with HDL-C < 42 mg/dl compared to those with HDL-C > 42 mg/dl (85.2% vs 71.8%, p < 0.05). AIP showed a strong correlation with triglyceride values exceeding 150 mg/dl and HDL-C less than 42 mg/dl and therefore we proposed that ratio of the two values could possibly be used as indicator for high prevalence of small, dense, LDL-C. Estimation of AIP could be used as a surrogate marker for the small, dense, LDL-C.

The CURES-8 being a pioneer study in context with pattern of dyslipidemia in Indian population, it will be interesting to know whether the authors can provide the AIP values in their subjects and its correlation with the estimated LDL particle size.

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Reply from the Author

Sir,

Owing to the marked increase in coronary disease in India, data on cardiovascular risk factors are of great importance. In our study on small dense LDL we had demonstrated the association of small dense LDL with coronary artery disease in Asian Indians and also suggested that triglycerides/HDL ratio of > 3.0 could be used as a surrogate marker for small dense LDL. The study done by Dr Uday Jadhav is in agreement with our findings as the Atherogenic Indes of plasma (AIP) used by them is the log transformed values of triglycerides/HDL ratio. Indeed as it is only a mathematical derivation of triglycerides/HDL ratio, one would expect to get the same results.

However, as suggested by Jadhav et al we did an analysis, to determine AIP and its correlation with LDL particle size. The AIP values in the diabetic subjects with (0.20) and without (0.13) coronary artery disease was higher than that observed in healthy normals (0.008). As expected both triglycerides/HDL ratio and AIP showed the same strong correlation with small dense LDL (r=0.728) and LDL particle size (r=-0.693). Similar to triglycerides/HDL ratio, the area under the curve for AIP for elevated small dense LDL (≥29.0 mg/dl) was high (0.885) and a value of 0.12 had the optimum sensitivity (79.1%) and specificity (78.9%) to identify small dense LDL. Corresponding values for a triglycerides/HDL ratio of 3.0 were sensitivity (80%) and specificity (78%) respectively.

Though both triglycerides/HDL cholesterol ratio and AIP showed a good correlation with small dense LDL, from a clinical point of view, using the former using triglycerides/HDL ratio would be simpler as the later involves conversion to SI units and thereafter logarithmic transformation of the same. Further, it is easier to determine a single cut off for triglycerides/HDL cholesterol ratio than AIP. However, owing to the skewness in triglycerides levels, it would be logical to use AIP in large epidemiological studies or while looking at the effect of intervention studies.

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REFERENCES

Does ISI of Thromboplastin Affect the INR Value?

Sir,

Prothrombin time is used to monitor oral
anticoagulant therapy for the prevention and control of thromboembolism. There is a significant variation in the patient response and a relatively narrow therapeutic window, and is associated with a significant risk of bleeding. The purpose of laboratory control is to maintain a level of hypocoagulability which effectively minimizes the combined risk of hemorrhage and thrombosis, which is referred to as the therapeutic range. There is a marked difference in sensitivity of commercial thromboplastin reagents to the anticoagulant effect of warfarin.1

The thromboplastin reagents used are assigned an ISI (International Sensitivity Index) value depending on their sensitivity to the anticoagulant effect of warfarin, the more sensitive reagents being characterized by low ISI values. The ISI quantifies responsiveness of a PT reagent to the anticoagulant effect of warfarin. The smaller the ISI value, more sensitive it is, to warfarin induced vitamin K clotting factor deficiency.2

Five hundred and ninety seven samples were tested over a one year period. Prothrombin time was performed using two different reagents, one thromboplastin reagent with a low ISI value of 1.26 and the second reagent with a high ISI value of 1.93 and the INR was calculated for each test.

A paired students t test was applied between the two data to assess the significance of difference if any. There was statistically significant difference between the two sets of INR data - the calculated t value was 0.05 for P<0.05. Statistically significant difference was also obtained in the INR value in the therapeutic range and in the INR range 3 - 3.9. However with higher INR values above 4, no significant difference was found.

Individual responses to oral anticoagulant treatment are variable and so must regularly and frequently be controlled by laboratory tests to ensure that the anticoagulant effect remains within the therapeutic range. Inter laboratory discrepancies in INR values are attributable to differences between automated instruments, interactions unique to specific reagent-instrument combinations, differences in citrate concentration of anticoagulant solutions and ISI value, specimen differences and inherent biological variations in an individual.

The choice of thromboplastin greatly determines the accuracy with which anticoagulant control can be maintained. If the ISI of thromboplastin is high, then a small change in PT represents a large change in the degree of anticoagulation. The more sensitive reagents have the ability to detect subtle changes in the levels of vitamin K dependent clotting factors. This may have a detectable, clinically significant difference in either the degree of anticoagulation or improved ability to monitor therapy.3 Most studies recommend the adoption of low ISI thromboplastin with ISI of 1.2 or less for monitoring patients on oral anticoagulant therapy.

This study involved comparing the results of INR obtained with reagents with 2 different ISI values and the INR values showed a statistical significance. It may therefore be inferred that the variation in the INR values obtained with the PT reagent with high ISI value will alter the clinical outcome, although a blinded prospective study is required to study the clinical outcome.

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Eratum

The following on page 309 column 2 last para should read Beta blockers, currently it says “a blockers”; on page 310 column 1 last para, should read Beta blockers, currently it says “a blockers”; on page 310 column 2 First para, should read Beta blockade, currently it says “a blockade”.

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