

Alcoholic and toxicologic aspects of carbohydrate deficient transferrin levels (CDT%) in percentage cases of toxic exposition

CDT% has been traditionally known to be related to the intensity of alcohol abuse and its duration. Some other factors are supposed to interact with CDT%, which may influence its role in the field of practical applications in differential diagnosis.

Methods: The purpose was to do screening among inhabitants of a Hungarian village as well as to measure the CDT% values among persons with professions with known toxic exposition. The author analysed more than 700 measurements of 667 persons performed during two years and selected 60 persons whose results had been influenced by toxic exposition. The measurements were performed with a ROCHE HITACHI MODULAR P 912 automatic machine.

Keywords: non alcoholic fatty liver, carbohydrate deficient transferrin

Introduction of the study

Aim of the study: Confirmation of alcohol abuse and toxic exposition as well as their differential diagnosis by the measurement of CDT%, AST, ALT and GGT.

Results: Normal values of MCV, ALT, AST and GMT together with negative anamnesis of alcohol abuse among women confirm that the elevation of CDT% may be a result of toxic exposition. Among men I also confirmed alcohol abuse or toxic exposition. In case the CDT % value exceeds 5–6% the probability of toxic exposition is higher than 80% in concert with the anamnestic data. The highest CDT% value measured among women was 8.4 and among men 16.6.

Conclusion: The probability of toxic exposition is currently very high. In concert with my results in case of extreme high CDT% results (i.e. higher than 5–6%) I can anticipate a toxic exposition. I point out the importance of less specific but very sensitive pretests by which I could identify the risk factors in time.

Abbreviations: GGT=gamma-glutamyl transpeptidase, ALT=alanine aminotransferase (GPT), AST=aspartate aminotransferase (GOT), CDT= carbohydrate deficient transferrin, MCV=mean corpuscular volume.

CDT% has been traditionally cited in the literature as related to the intensity and quality of alcohol abuse and its duration [1, 2, 3, 4]. During the verification of alcohol abuse several modifying factors emerged. It is not an accidental fact because ethyl alcohol is only one of the many chemical toxins we get in touch with [6, 7, 8, 9, 10, 11, 12].

Patients and methods

The inhabitants of the Hungarian village Enese were analysed because they had chemical exposition in their anamnesis. Persons participating in the study had given their informed consent to the measurement of CDT% and the routine laboratory parameters. The epidemiologic study was performed with the consent of the Health Scientific Committee and the Ethical Committee of the Regional Research (nr. 76/1–19/2006) after 700 measurements of 667 persons. The measurements were performed between December 2005 and December 2006. In the current study we selected 60 patients with certain chemical exposition according to their known 31 laboratory parameters as well as 11 morbidity and sociological data. Professional exposition to chemical toxins was also confirmed by the anamnesis of patients. We could only partially acquire the exact list of compounds and the verified concentration of the chemicals because patients feared their employers and their dismissing.

Some persons withdrew their consent in spite of the fact that we had given them our assurance that they could remain in anonymity. The great majority of employers refused to cooperate and find the reasons of toxic exposition. The group of patients consisted of 40 men (their age was 46.1 years on average) and 20 women (their age was 48 years on average). We took into account sex, age, height, weight, race, characteristic features of the occupational toxic exposition, personal anamnesis, health status, smoking and drinking habits, possible presence of other abuses and also the drug anamnesis of the patients. In this study we analysed values of MCV, GGT, AST and ALT according to CDT%.

METHODS: The difference among transferrin isoforms consists in their electric charge because sialic acid has a negative electric charge. By this fact it is possible to distinguish the forms of CDT by the proportion of sialic acid. Liquid Chromatography or HPLC increases the sensitivity of the method by the use of anion changing columns. This way it is easier to distinguish di- and trisialo transferrin isoforms from asialo-, monosialo-, tetrasialo- and pentasialo ones. Technically it is very important in the situations when a high proportion of trisialotransferrin isoform is present. HPLC Biorad CDT% kit produced commercially is capable of measurement of the relative proportion of different transferrin isoforms being present in the serum. There is a strong correlation between the results gained by using the Biorad %CDT TEST Assay and the traditional CDT% Test Assay. The N Latex CDT Immunoassay developed in the last time is much more specific than the column separation technics because it filters the disturbing effect of the genetic variants¹.

The up to date immunoturbidimetry test may be performed among the daily routine measurements because after the anion changing separation it is possible to measure the exact amount of CDT. This way we count the CDT% level from the proportion of the soluble transferrin and the total transferrin. We used the second generation Roche test provided by Roche diagnostic GmbH Mannheim with the use of the “Roche Hitachi Modular p912 automat” in the Central Laboratory of Kaposi Mor Hospital [13,14].

RESULTS: There were 60 men in the group of patients (age 46.1 on average, CDT% 4.82 on average (minimum value 1.82 CDT%, maximum value 16.6 CDT%). The difference between the reference value measured for the Hungarian population (2.2–2.35 CDT% in abstinent and in persons with age between 18 and 65 years drinking less than 60 gr. of ethyl-alcohol per week) and the measured minimum and maximum values were -0.39 and 14.4 respectively. [15]

The MCV was 95 femtoliter on average, the minimum value was 87 femtoliter, the maximum value was 104 femtoliter. The GGT was 92.2 U/L on average, the minimum value was 38 U/L, the maximum value was 508 U/L. The AST was 55.9 U/L on average, the minimum value was 33 U/L, the maximum value was 500 U/L. Information about the technology could be given by Roche/Hitachi 904/911/912/917, Modular P: ACN 276.

The ALT was 61 U/L on average, the minimum value was 19 U/L, the maximum value was 445 U/L. It can be concluded from the MCV, GGT, GPT and GOT values of male patients that many of them suffer from alcoholism.

There were 20 women in the group of patients (CDT% 4.21 on average (minimum value 1.57 CDT%, maximum value 8.43 CDT%). The difference between the reference value counted for the Hungarian population (2.2–2.4 CDT% in abstinent women between 18 and 75 years) and the measured values was +1.954 CDT% on average, minimally: -0.53 CDT%, and maximally: 6.23 CDT%. The MCV was 89 femtoliter on average, the minimum value was 86 femtoliter, the maximum value was 96 femtoliter. The GGT was 30.9 U/L on average, the minimum value was 18 U/L, the maximum value was 44 U/L. The AST was 21 U/L on average, the minimum value was 13U/L, the maximum value was 28 U/L. The ALT was 20 U/L on average, the minimum value was 10 U/L, the maximum value was 26 U/L. The MCV, GGT, ALT and AST values were in normal range in women, from which it can be supposed that they are abstinent. Reference ranges counted for the Hungarian population and the anamnesis support this assumption. [15]

DISCUSSION: According to our current knowledge the combination of CDT%, MCV and GGT level is the best way to verify latent alcoholism. In accord with our preliminary studies we consider the sensitivity and the specificity of the common use of CDT%, MCV and GGT for the latent alcohol abuse in accord with literature as approximately 85–95%. [17,18.] There were frequent and severe paradoxes between the anamnesis and the laboratory parameters taking into consideration the intensity of alcohol abuse of the 667 examined persons during the 700 measurements. Several times a high level of CDT% was

measured among total abstinent. The normal values of MCV and GGT (in spite of the high levels of CDT%) confirmed that the analysed person did not suffer from alcoholism. During the detailed anamnesis chemical toxins were found to be present in the professional anamnesis of many patients. [19] There were extremely high levels of CDT% in persons working with organic solutions as well as with agricultural chemicals. It is well known from the literature that different chemical toxins are harmful for the liver function and the production of blood cells in the bone marrow. Routine measurement of CDT% could be used as a screening method of these toxins in spite of the fact that their exact chemical structure is not known. [10,11,12]

Other factors are also supposed to influence the toxic status of alcohol abusers. [12] During the detailed anamnesis we could select a group of 60 persons who had been exposed to chemical toxins in professional conditions. Members of the group formed a heterogenic group from all aspects because we had not been able to acquire adequate information about the exact toxic anamnesis of patients that would help us to differentiate the toxins. We tried to collect as much anamnestic and heteroanamnestic data about the analysed persons as it were possible. The complete list of the collected chemical toxins consists of agricultural protective agents, eg. emidosulfurone, jodosulphurone, beterontrikombate, bromoximil, cyclodixime, 2,4-D, 2-4d-florosulone, dicombe triflurone, 3-6 dichlor-pikolinat, dimetimide, pendimetleline, dikvate dibromid, forensulphurone, imezomax, isoxaflutale, dopapisochlor, terbutalezine, L- fluorchloridon, tribenzodine, methyllimusate, mesotriene, tritosulphurone, dicombe-trimesosulphurone, cipermetrine, tephentrinkarboxime, chlorpirphane, carboxitherine, flurilezol, fenoxate+midkorbexime, dinikonezile, pikoximetalone, pregoverine, elusilezol, karbendezintiophenat-methyl, polyethylenoxid, polyakrylamide kopolimer, izoderil-methylated etoxylate, testosteronenantate and testosteroncipronate.

Organic detergents, lacquers on water base, anilin pigments, toluene, benzene, hair lacquers with benzylbenzoate, aliphatic and aromatic amines, alkylbromide, tetrahydrofurane; dimethyl-formamide, ethanol, dichloro-ethane, acetone, chloroform ethylacetate hexane, izooxazoline, aza-indole, imidazopyridine.

From these results it could be concluded, that MCV and transaminase levels exceed the normal values several times in the group of men. Multiple increases of AST, ALT and GMT together with the increase of MCV confirmed that the analysed men had been alcohol abusers drinking in amounts frequently exceeding the daily dose of 60 g. Alcohol abuse was also confirmed by the anamnesis. [21,22] With male patients CDT% exceeding the level of 3% together with MCV exceeding 96 femtoliters was observed, which confirms the fact of alcohol abuse. Simultaneously with CDT% exceeding the level of 5.5% MCV exceeds 104 femtoliters. Increase of AST and ALT could be observed only with CDT% exceeding the level of 15%. The value of GGT increases 7–12 times only near the level of CDT% exceeding 13.4%. Currently we are not able to answer the question con-

cerning the exact biochemical effect of alcohol and chemical toxins on the potentiation of CDT% level. The data acquired from 1300 measurements shows that the daily alcohol use between the age of 14 and 75 years in patients with CDT% between the level of 2.2 and 2.4 is under 40 g. As alcohol abuse exceeds the daily dose of 40–60 g., CDT% increases up to 2.4% in women and up to 2.8% in men. [15] Figure 1.

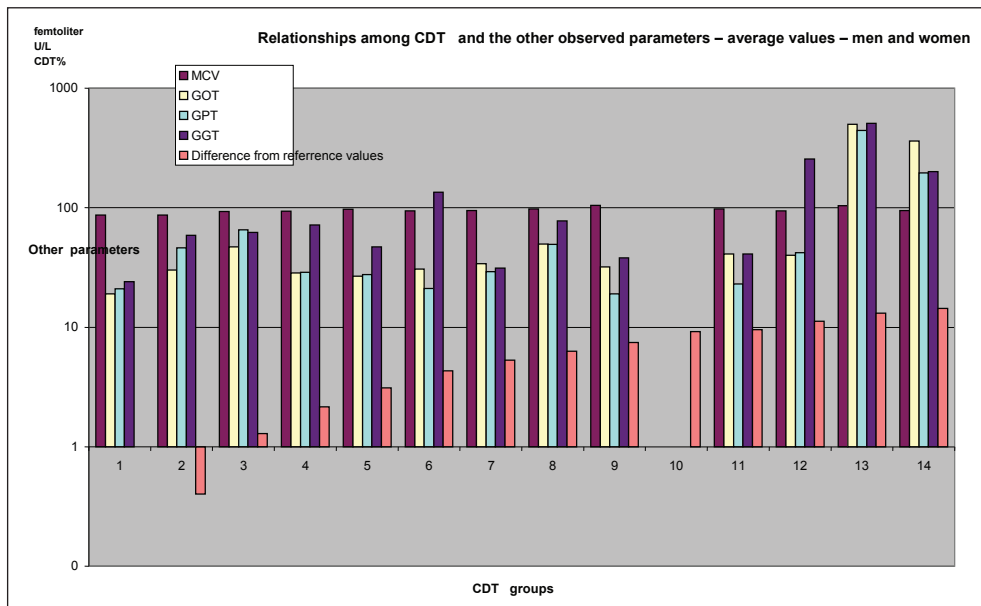


Figure 1: Relationship among CDT – and the other observed parameters – average values – men and women (own source)

Scientific works usually specify alcoholism at the daily use of approximately 60 g. alcohol. According to our measurements this amount brings about the increase of CDT% over the level of 2.8% among men and over the level of 2.4% among women in 95% of the cases [15]. The level of CDT% increases after an alcohol abuse that is permanent or that lasts at least 3–4 weeks in doses higher than 60 g. in 95% of the cases. Sometimes longer periods of the necessary alcohol abuse were measured. The enzyme inducing effect of chemical toxins starts at the level of about 5–6% CDT. Chemical toxins are the crucial factors causing the robust increase of CDT% over the levels of 5–6 CDT% in male as well as in female patients. In women MCV and transaminase levels are in normal range, consequently, alcohol abuse may be excluded. Linear elevation of CDT% levels is not followed by the elevation of MCV, ALT, AST and GGT, which confirms our assumption that chemical toxins are the cause of the significant CDT% increase or it may be expected that CDT% is the only marker of the toxic effect. Figure 2. – 3.

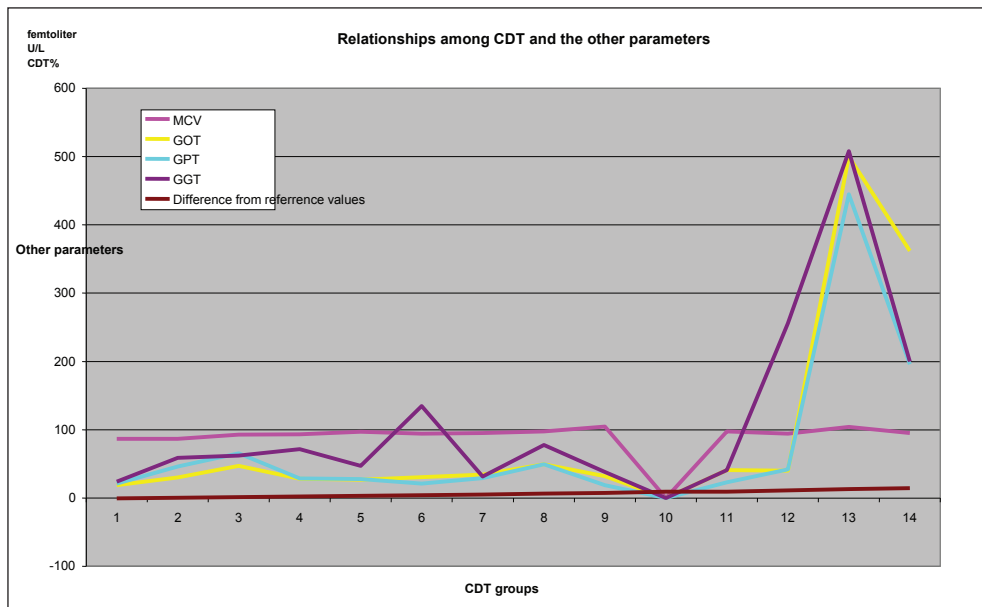


Figure 2: Relationship among CDT - and the other observed parameters (own source)

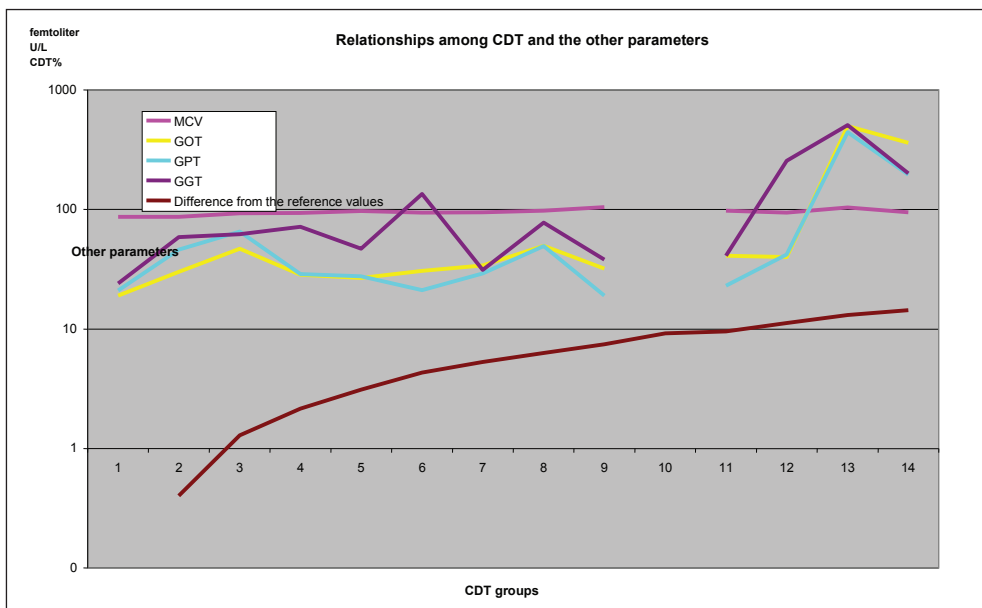


Figure 3: Relationship among CDT - and the other observed parameters (own source)

Contrary to men, the increase of CDT% level was continuous in women. Increase of MCV, GGT, ALT and AST was not parallel to it, consequently, the influence of alcohol abuse may be excluded and it can be supposed that the only cause of its significant in-

crease was alcohol abuse mentioned in the anamnesis. It should be pointed out that the highest level of CDT% was 8.43 among women and 16.6 among men. We agree that the fragment measurement of chemical exposition is very difficult. Toxic effects caused by malnutrition connected with the social position of the analysed persons also belong to this topic. [20, 24, 25] It is definitely visible that markers used for verification of alcohol abuse did not follow the increase of CDT% level linearly and significantly, which demonstrates that the phenomenon is caused by toxic exposition and not by alcohol abuse. [25]

The analysis of CDT% levels shows that it could have an important role in the analysis of alcohol abuse as well as in the detection of chemical exposition in clinical medicine, in insurance medicine, in forensic medicine and in military medicine because it may be used as a pretest, especially in the range exceeding the level of 5–6 CDT%. Probably because alcohol could be listed in the category of chemical toxins a lot of directors of laboratories dealing with chemical toxins suppose that alcoholics tolerate rough conditions better than abstinent. [26] Psychologically it could be partially true but somatic damage could not be avoided and separate monitoring is difficult. Figure 4.–5.

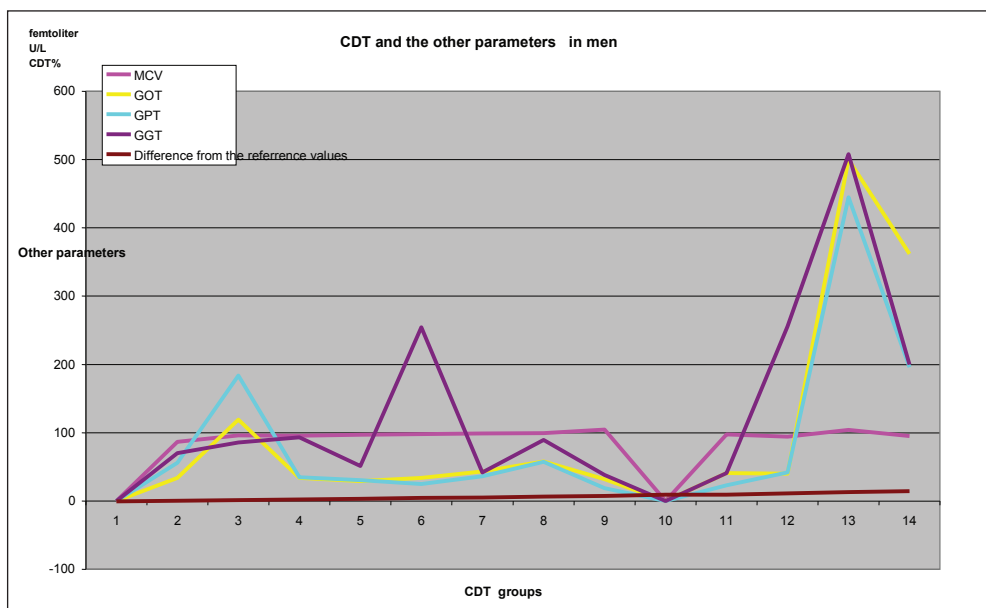


Figure 4: CDT and other parameters in men (own source)

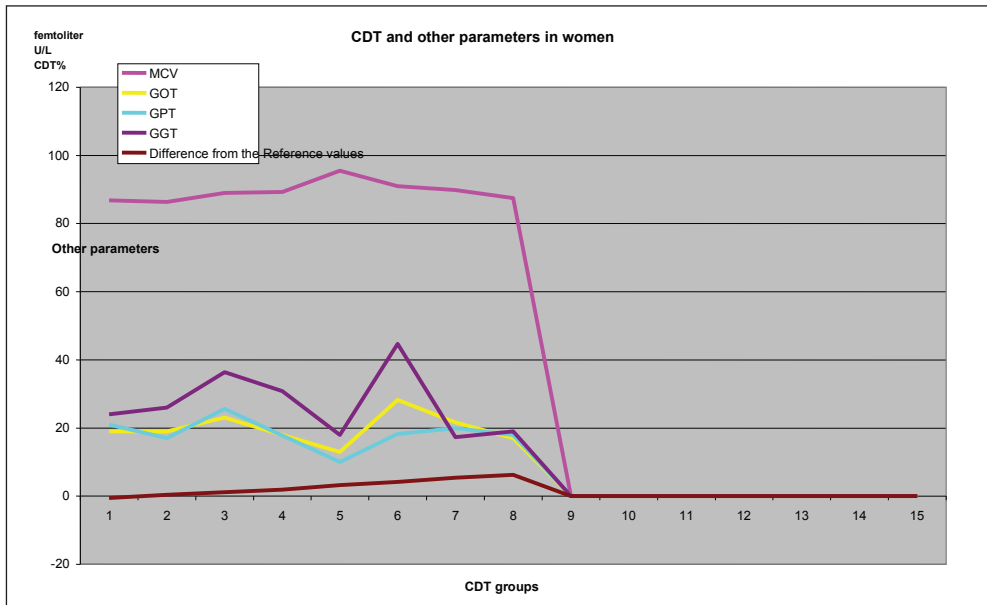


Figure 5: CDT and other parameters in women (own source)

Conclusion

CDT% may play an important role in the evaluation of alcohol exposition intensity as well as in the detection of the influence of chemical toxins. During more than 700 measurements performed in 667 persons we observed an extreme elevation of CDT% level in a group of 60 patients.

Because of the relatively small number of patients in our group we need more measures differentiating and specifying the effect of chemical toxins. Analysis of the biochemical mechanisms of various chemical toxins may contribute to the observation of the immune system as well.

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A szénhidrátszegény transferrinszint (CDT%) százalékos kimutatása vegyszerexpozíció esetén alkohol és toxikus hatás szempontjából

SZABÓ GYÖRGY

A CDT% szint hagyományosan ismert összhangban van a túlzott alkoholfogyasztás intenzitásával és időtartamával. Az utóbbi időben néhány tényező – mint az alkoholfogyasztás tényének igazolása – miatt elvárják, hogy kimutatható legyen a CDT% szint, ami hatással lehet egy adott területen végzett tevékenységre a gyakorlati alkalmazás differenciáldiagnózisakor. Ezen szűrések célja a magyar falvak lakosainak körében mérni a CDT%-értékeket a vegyszerexpozíció terén érintett szakmák ismert mérgező hatásai és az alkoholfogyasztási szokások tekintetében. A szerző több mint 700 mérést elemzett két év alatt, melyet 667 főnél végzett, és kiválasztott 60 személyt, akiknek eredményeit nagyban befolyásolta a kimutatható toxikus hatás. A mérések végzéséhez ROCHE HITACHI MODULAR P 912 automata gépet használtak.

Kulcsszavak: alkoholmentes zsírmáj, szénhidrátszegény transferrin