

Early Repolarization is Associated with Short QT Syndrome in Italian Cohort

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Background: Early repolarization (ER), defined as an elevated slurring or notching of the QRS-ST junction, or J wave, on electrocardiogram, has recently been linked to malignant ventricular fibrillation. Because ER is common in the general population, however, there is a need to identify when the pattern has prognostic significance. The early repolarization pattern may be associated with arrhythmogenic syndromes, specifically Short QT Syndrome (SQTS), a lethal disorder whose natural history is incompletely characterized.

Methods: The aims of this retrospective cohort study were to compare the prevalence of early repolarization and characteristics of J waves in SQTS patients and healthy controls, as well as assess whether the early repolarization pattern was associated with arrhythmic events in SQTS patients. The study population included 73 patients diagnosed with Short QT Syndrome and 146 age- and gender-matched healthy controls. Our group of SQTS patients at the Fondazione Salvatore Maugeri in Pavia, Italy represents the largest cohort described thus far. Early repolarization was stratified according to the amount of J point elevation, ≥ 0.1 mV or ≥ 0.2 mV, in inferior or lateral leads. Symptomatic SQTS patients were defined as those who had experienced syncope or sudden cardiac death.

Findings: The early repolarization pattern with a J point elevation of 0.2 mV or more was more prevalent in the SQTS cohort (16.44%, n=12) than in healthy controls (6.33%, n=10) (odds ratio, 2.892; CI 1.252 to 7.111). Among the SQTS cohort, however, there was no association between early repolarization and history of arrhythmic events. J wave duration with a J point elevation ≥ 0.2 mV in both groups of SQTS patients was longer than that of controls (46ms in symptomatic group, 37ms in asymptomatic, and 29ms in controls), but J wave duration was not significantly associated with symptomatic SQTS (p=0.0861). No other significant differences in morphological characteristics of early repolarization were found between symptomatic SQTS, asymptomatic SQTS and health controls.

Interpretation: J point elevations ≥ 0.2 mV were associated with SQTS, suggesting this elevation may have greater prognostic significance for arrhythmogenic disorders. The early repolarization pattern itself, however, does not represent a prognostic indicator for SQTS.

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Influence of Smokeless Tobacco Use on Diet and Nutrient Intake among Households in Bangladesh

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Background: Tobacco users on average have less adequate diet as compared to non-users. While the majority of the studies are from developed countries, less is known about the influence of tobacco on dietary composition in developing countries where malnutrition is a major public health challenge. Additionally, the effect of smokeless-tobacco use on dietary composition are unknown.

Methods: We used the nationally representative Household Income Expenditure Survey (HIES-2010) from Bangladesh. Detailed dietary data including both ethnic and regional specific foods were collected for 14 days and comprised of 7 visits with two days' recalls.

Findings: Overall, 71% of the households reported expenditure on tobacco (smoking and/or smokeless), and were considered tobacco users. Out of 12240 households, 2061 used smoking tobacco only (16.8%), 3284 used smokeless tobacco only (26.8%), and 3348 were dual-users (27.4%). After controlling for household expenditure, household size, place of residence, and education, smokeless-tobacco user households consumed significantly lower mean per capita daily total calories ($\beta = -342.88$; $p < 0.0001$) as compared to non-users. Dietary analyses revealed smokeless-tobacco users consumed significantly lower daily mean per capita of vegetables ($\beta = -19.65$ g/day; $p < 0.0001$), milk and dairy ($\beta = -9.81$ g/day; $p < 0.0001$), fish ($\beta = -9.84$ g/day; $p < 0.0001$), meat ($\beta = -10.9360$ g/day; $p < 0.0001$), legumes ($\beta = -3.23$ g/day; $p < 0.0001$), eggs ($\beta = -1.60$ g/day; $p < 0.0001$) as compared to non-users. However, mean per capita daily intakes of cereal products ($\beta = 39.26$ g/day; $p < 0.0001$) was significantly higher among smokeless-tobacco users as compared to non-users. Corresponding to these profound dietary differences, the intake of total dietary protein ($\beta = -10.01$ g/day; $p < 0.0001$), dietary fat ($\beta = -27.55$ g/day; $p < 0.0001$) were significantly lower, and dietary carbohydrate ($\beta = 94.32$ g/day; $p < 0.0001$) was significantly higher among smokeless-tobacco users as compared to non-users.

Interpretation: Smokeless tobacco user households in Bangladesh have poor diets and inadequate nutrient intake as compared to tobacco non-users. The study provides evidence to inform policy for addressing dietary inadequacy and malnutrition burden among smokeless-tobacco user households in Bangladesh.

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New Molecular Evidence of Exposure to Aristolochic Acid in South Korea: Implications for Global Public Health Hazard Linked to Nephrotoxic and Carcinogenic Herbal Medicines

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Background: Aristolochic acid (AA) is a potent nephrotoxin and carcinogen (IARC Group 1) associated with urothelial, hepatobiliary, and renal carcinomas. Exposure to AA from dietary intake of traditional herbal medicines containing *Aristolochia* species poses

a global health hazard, yet also an opportunity for disease prevention. Molecular epidemiology studies employing sensitive and specific biomarkers for screening of populations at risk are thus warranted.

Genome-scale studies established a characteristic mutational signature of AA. Exploiting its unique features (predominant A>T transversions), alongside the knowledge of key affected cancer genes, we devised a cost-effective targeted resequencing (TRseq) method to detect AA exposure in upper tract urothelial carcinoma (UTUC) samples from South Korean patients. *Aristolochia* species (e.g., *A. contorta*, Bunge) are included in the Korean traditional pharmacopoeia although the local occurrence of AA-associated cancers remains unexplored.

Methods: DNA from archived, paired kidney and UTUC samples of 16 Korean patients was used for adduct and TRseq analyses. 31 cancer genes, previously found recurrently mutated in AA-induced UTUCs from Asia and Europe, were selectively captured using Seq-Cap EZ enrichment kit (Nimblegen) and sequenced using Illumina MiSeq. Sets of UTUCs from Croatia harboring AA signature and UTUCs from US patients (unlikely to be exposed) were included as respective positive and negative controls. Somatic variants were called against the patient-matched non-tumor DNA.

Findings: Three of sixteen kidney samples tested positive for aristolactam-dA (AL-dA) adducts, indicative of past exposure to AA. A>T-positive UTUC samples were detected in 5 cases, 2 of which were also adduct-positive. Positive control samples exhibited a strong A>T signal while the US samples were A>T-negative, as expected.

Interpretation: The TRseq approach can detect AA exposure in UTUC tumors, providing a sensitive complement to the AL-dA adduct analysis. Furthermore, the presence of adducts and AA signature in South Korean UTUC cases highlights a previously uncharacterized population at risk. The future use of TRseq, either alone or in combination with adduct analysis, can address exposure to AA, thereby assisting in the design of preventive measures against this global public health hazard.

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Substance Abuse, A Challenge to the Mental Health Status in Uganda

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Background: Globally, it is estimated that in 2012, between 162 million and 324 million people has used substances. In Uganda, there is 79% increase in use and abuse of substances, and substances commonly abused are alcohol, cannabis, tobacco, khat and kuber. The global burden of disease report for Uganda of 2010 indicates alcohol, cigarette smoking and drug use as one of the fifteen leading causes of disease. Hence this study assesses the risk factors associated with, the prevalence rates and the effects of substance abuse on the mental health status of Ugandans.

Methods: Literature review of the World Drug Report (WDR) 2006, Ministry of Health Uganda (MoH) reports, Uganda Youth Development Link (UYDEL) report on substance abuse of 2010, newspaper articles and journals.

Findings: According to the UYDEL report of 2010, the risk factors associated with substance abuse include parental influence and friends while other studies from different journals show permissiveness and psychological stress. According to the WDR of 2006, the prevalence rates of alcohol use are 23.7%, cigarette smoking is 20.4%, cannabis is 1.4%, opioid use is 0.05%. From the MoH reports, 25% of mental health cases received at Butabika National Mental Referral Hospital between February 2015 and March 2015 were due to substance abuse.

Interpretation: A relatively large number of mental health cases attributed to substance abuse were received at Butabika National Mental Referral Hospital. Most people are introduced to substances by their parents. Alcohol has the highest prevalence rate among the abused drugs. Therefore, there is a need to increase effort by government, the religious community and civil society towards curbing substance abuse.

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Global Development-Related Assistance for Mental Health: A Review of the Last Decade

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Background: Mental and behavioral disorders constitute 7.3% of the global burden of disease and are projected to be the leading cause of disability in the year 2030. This burden is disproportionately borne by low- and middle-income countries. Recently, global mental health has gained international attention, as evidenced by the inclusion of mental health and wellbeing in the Sustainable Development Goals, the international meeting on mental health as a priority for global development-co-hosted by the World Health Organization and the World Bank in April of 2016—and other key milestones. This new attention to mental health is expected to generate additional financial resources for care, not only at the country level, but also at the international level. However, the current contributions of the international development community to fund programmes to support mental health globally is poorly documented.

Methods: The research directly addresses this knowledge gap by systematically analyzing development-related assistance for mental health over the past ten years, 2005–2014, including support from development partners, NGOs, foundations, and the pharmaceutical industry. The nature of the types of projects and programmes funded are assessed. The analysis separates funding for research from funding for programmes, as the nature of funding for research is geared primarily towards knowledge creation as opposed to increased access to services.

Findings: The analysis finds very limited financial support for mental health care (in comparison to other key areas for global health), and an almost complete lack of focus on mental health