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Metabolites and lipoproteins profiles of a cohort of Pancreatic Ductal Adenocarcinoma patients and associated immune responses.

Pancreatic Ductal Adenocarcinoma (PDAC) is one of the most fatal cancers with the poorest 5- year survival rate of 9%. PDAC is usually asymptomatic at the early stage and most patients are diagnosed at the advanced stage. The discovery of biomarkers at the resectable stage could be vital in improving the survival rate as well as improving the treatment strategies. This study aimed to identify metabolites and lipoproteins as well as associated immune cells/markers and their possible roles in PDAC. Following informed consent, blood samples were collected from 34 PDAC patients consisting of 22 resectable, 8 locally advanced and 4 metastatic pancreatic cancers (RPC, LAPC and MPC respectively) and 6 chronic pancreatitis patients at Chris Hani Baragwanath Academic Hospital. Six healthy volunteers were included, and the blood was processed into serum, plasma, and peripheral blood mononuclear cells (PBMCs). Nuclear Magnetic Resonance (NMR) spectroscopy, LipoScale test and Spectrophotometric assays were conducted on serum. A lipoprint assay was carried out to determine lipoprotein parameters and the lipid concentrations of each subtype. Multi-colour flow cytometric immunophenotyping and real-time PCR analyses were used to assess the immune cell markers. Data analysis was done using the R software and R studio and the Wilcoxon and Kruskal–Wallis rank-sum tests were used to compare differences in numerical covariates. Spearman's rank test was used to calculate the correlation coefficient (rho) between variables and the Wald test was used to calculate the statistical significance (*p*-value) of the differences between the Kaplan–Meier survival curves. In this study, the results showed elevated levels of glycine and lactate with worsening tumour stage. Decreased ethanol and 3-hydroxybutyrate concentrations were independently associated with longer survival time, irrespective of tumour stage. Abnormal lipoprotein associated with dysregulated lipid metabolism was detected. Glucose, lactate and some lipoproteins were directly linked to inflammatory markers. Furthermore, PDAC severity is associated with elevated levels of ROS. PDAC patients with CD4/CD8 ratio of less than 1 survived longer (Hazard Ratio = 3.572 *p*-value = 0.049). In this study identified novel metabolites such as 3-hydroxybutyrate and ethanol as well as $CD8^+$ T-cells were shown to be associated with patients' survival. Furthermore, evaluating the lipoprotein profiles might be vital in predicting prognosis and informing treatment decisions. This study showed that the integration of metabolomics, lipoproteins, and immune cell networks can contribute to a better understanding of the biology of PDAC in the population group.