Charles University was founded in 1348 during the rule of King of Bohemia and Holy Roman Emperor Charles IV. It became the first Studium generale north of the Alps and east of Paris. Modelled on universities in Bologna and Paris it quickly gained international renown. Originally, it had four faculties: theology, liberal arts, law, and medicine. The status of status of Czech academic community was strengthened under Charles' son, King Wenceslas IV.

The university underwent transformation during the Hussite reformist movement (which preceded the Reformation); the religious reformer Master Jan Hus was rector of the university at the time. During the social and political revolution that followed, the university was reduced to just one faculty - the Faculty of Liberal Arts (Facultas artium liberalium), becoming a prototype for later Reformation academies.

Habsburg Emperor Rudolf II turned Prague into a cultural metropolis where the university flourished alongside the court. In the early 17th century, the university fell under the strong political influence of the Protestant Czech Estates involved in the anti-Habsburg opposition movement, whose representatives sparked what grew into the Thirty Years' War that ultimately engulfed most of Europe.

The outcome of the war saw fundamental changes and the institution became a part of Charles-Ferdinand University (a name which persisted until 1918). All four pre-Hussite faculties were restored and the university was transformed into a state-governed educational institution. This process culminated in the 1780s with reforms introduced by Emperor Joseph II.

Following the reforms of 1848-49, the university began to assume the form of a modern higher education institution. In 1882, at the culmination of the Czech National Revival, Prague's Charles-Ferdinand University was divided into two institutions: Czech and German.

By the turn of the 20th century, both universities had achieved a high academic standard. One of the professors at the German University was theoretical physicist Albert Einstein. The academic staff at the Czech University included respected figures who played a prominent role in the process of national emancipation – most notably Professor Tomáš G. Masaryk, who in 1918 became the first President of Czechoslovakia.

Charles University - the name given to the Czech university after independence – achieved results putting it on a par with the world’s most prestigious academic and research institutions. A noteworthy example is Professor Jaroslav Heyrovský's inventions in polarography, for which he was awarded the Nobel Prize in 1959.

The occupation of the Czech Lands by Hitler's Germany brought much hardship and great losses. On 17 November 1939, all Czech higher education institutions were closed in response to student demonstrations on 28 October 1939 and during the funeral of the medical student Jan Opletal; this was followed by widespread persecution of university students and teachers.

Charles University was unable to resume its activities until after the Second World War. With the end of the Nazi German Reich, the German University in Prague, which in 1939 had joined an alliance of Reich universities, also ceased to exist.

The renewal of free academic life at Charles University was interrupted by the communist coup of 1948. For many years to follow, the regime subjected education and research to tight ideological and political control; this naturally had a detrimental effect on international links and research opportunities. Students, loyal to their tradition of academic freedoms, demonstrated on 17 November 1989 against the totalitarian regime, eventually initiating its fall.

Modern university life began to thrive, drawing strongly on international cooperation. Aware of its mission, Charles University continues to nurture academic cooperation and plays an active role in a broad spectrum of European and global programmes.