harapan dan angan-angan beliau menjadi kesampaian pada pendidikan saya sampai saat ini.

Semoga isi tulisan pada penelitian ini memberikan manfaat bagi kesejahteraan umat manusia, selanjutnya diberikan barokah, karunia, taukhid dan hidayahNya untuk kebaikan sesama umat manusia. Aamiin.

RINGKASAN

Cacat lahir (*birth defect / congenital defect / congenital condition*) adalah kelainan yang muncul pada saat lahir dan dapat menyebabkan kecacatan fisik, mental atau kematian. Cacat lahir ini dapat berdampak pada kelainan struktur, fungsi atau metabolisme. Setiap tahun kira-kira 7,9 juta anak di seluruh dunia (kira-kira 6% dari seluruh kelahiran di dunia) dilahirkan dengan cacat lahir yang serius akibat kelainan genetik atau penyebab pasca konsepsi lainnya seperti alkoholic, rubella, sifilis, defisiensi yodium dan sebagainya. Di Indonesia kelainan congenital merupakan salah satu dari banyak penyebab kematian bayi baru lahir dan apabila tidak ditangani secara cepat dan tepat, maka kelainan congenital akan menjadi cacat seumur hidup yang dapat meningkatkan angka kesakitan dan kematian bayi di Indonesia (Depkes, 2010).

Congenital Bilateral Absence of Vas Deferens (CBAVD) adalah salah satu cacat lahir dengan ciri azoospermia yang berakibat terjadinya infertilitas, namun apabila tidak ditangani, akan memicu masalah terutama keutuhan suatu rumah tangga. Perkembangan penelitian tentang CBAVD di tingkat internasional telah dimulai sejak tahun 1968, dengan ditemukannya seorang pria Amerika yang meninggal dengan sebab adanya abses yang membesar di *scrotum* dan terbentuknya sistik fibrosis yang sudah metastasis berbagai organ, utamanya: pankreas, paru-paru, liver, yang diduga meninggalnya berhubungan dengan immunodefisiensi (Wang, 2002). Pengembangan program skrening telah digalakkan sesuai dengan tingkat melajunya kasus CBAVD dengan dilakukannya

"*Preconception and Pranatal Carrier Screening for Cystic fibrosis*" pada tahun 2001 untuk penderita *carrier* CBAVD. Hal tersebut juga dilakukan pada bayi yang baru dilahirkan untuk dilakukan *Newborn Screening* melalui "*Initial Screening test level of IRT (Immunoreactive Trypsinogen*)" (Cocuzza, 2013). Diharapkan hasil mutasi ΔF 508-T gen *Cystic Fibrosis Transmembrane Conductance Regulator* **(**CFTR**)** dari orang Indonesia akan disesuaikan dengan hasil mutan ΔF 508-T gen CFTR yang terjadi pada orang kulit putih (orang Eropa) yang hidup dalam iklim sub tropis, sehingga prevalensi yang tinggi dari kasus CBAVD sangat dipengaruhi oleh etnisitas.

Tujuan jangka panjang penelitian ini adalah untuk mengetahui berapa base pair dari penyakit CBAVD di Indonesia yang diharapkan sebagai prototype untuk memperbaiki gen yang mengalami mutasi akibat defek congenital. Keberhasilan penelitian ini dapat memberikan solusi terhadap problem penyakit CBAVD pada defek congenital akibat mutasi ΔF 508-T gen pengkode CFTR. Manfaat penelitian ini ialah memberikan informasi baru bahwa CFTR berperan penting dalam terapi CBAVD dan berat molekul protein mutan ΔF 508-T gen pengkode CFTR sebagai prototype pada penderita CBAVD di Indonesia serta merupakan data dasar untuk penelitian berikutnya yang berbasis pada pendekatan molekular.

Pada penelitian ini membuktikan bahwa: (1) kelainan cacat congenital CBAVD pada orang Indonesia memiliki panjang rantai DNA gen CFTR sekitar 400 base pair (400bp), sedangkan pada orang Eropa 650 bp, sehingga lokasi mutan ΔF 508-T gen CFTR sangat tergantung etnisitas, (2) 3 primer yang berbeda dimulai holding pada siklus yang ke-4 dan terus terjadi peningkatan sampai siklus

yang ke-40 sebagai gambaran profil cDNA dari penderita CBAVD di Indonesia, (3) Perbedaan hasil PCR kemungkinan dipengaruhi jumlah sampel yang diteliti, teknik pelaksanaan penelitian yang meliputi waktu dan suhu saat *annealing*, serta sikling replikasi, dan (4) hasil analisis SDS-PAGE untuk penentuan berat molekul protein CFTR pada: ± 190 – 250 kDa, 170 – 180 kDa, 140 – 160 kDa, dan 120 kDa.

SUMMARY

THE POTENTIAL OF ΔF 508-T GEN MUTANT THE CODING OF CYSTIC FIBROSIS TRANSMEMBRANE CONDUCTANCE REGULATOR (CFTR) AS PROTOTYPE AT THE CONGENITAL BILATERAL ABSENCE OF VAS DIFERENS (CBAVD) DISEASE IN INDONESIA

Maslichah Mafruchati

Birth defect (congenital defect or congenital condition) is an anomaly appearing at birth and able to cause the physical or mental defect or death. Birth defect generally can be detected during the prenatal period. However, if this cannot be detected during the prenatal period, it can be identified at the post natal examination. This congenital defect can bring impact to the structural, functional and metabolism anomalies. Every year, approximately 7.9 million children in the world (about 6% of the whole anomalies in the world) were born with serious congenital defects due to genetic anomaly or other post-conception causes, such as alcoholic, rubella, syphilis, iodine deficiency and the like. Aacording to Center for Disease Control and Prevention (CDC), in US there are about 3% children born suffering from various congenital defects will die on their first year of living. The congenital defect in Indonesia constitutes one of the causes of death of new born babies and if it is not handled properly and quickly, it will become the life long defect able in to increase the rates of sickness and mortality of babies in Indonesia (WHO, 2010).

Congenital Bilateral Absence Vas Diferens (CBAVD) is of one the congenital defects characterized by **azoospermia** causing the occurrence of **infertility**. Infertility in men is still the case not yet having been completely and thoroughly handled in Medical Science. Therefore, it is not only prioritized to do the genetic test to the patient. Also, the etiology *identification* as well as *the counseling* shall have been socialized in order to prevent the transmission of genetic defect through **assisted Reproductive Technology (ART)**. The rate of CBAVD occurrence is certainly very small, namely around 2-10%. However, if it is not properly handled, it will trigger the occurrence of a problem, particularly the good harmony of a household. The infertility identified by azoospermia can be corrected through the surgery and non-surgery actions. However, the surgical action still requires further experience and research. In addition, there are many congenital defects unable to be given a therapy or die at the early ages. Congenital defect can also cause the occurrence of *mental disorder*.

In Washington, the CBAVD cases are mostly dominated by the White-men. Based on this case, a research was conducted at **Pasteur Institute** in 1983 and it found out that the possible cause of this case was CBAVD. The **Diagnostic Research** was developed and it produced a **Genetic Test Kit** acknowledged by

FDA at Robert Gallos Laboratory in 1985. The screening program development has been activated pursuant to the speed rate of the CBAVD case by performing "**The Preconception and Prenatal Carrier Screening for Cystic Fibrosis**" in 2001 for the patient of CBAVD carrier. This was also conducted to new born babies to perform the **Newborn Screening** through "**Initial Screening Test Level of IRT (Immuno Reactive Trypsinogen).**" In 1989, "***Gene Testing Going Mainstream***" was invented to detect the presenceof gene mutation caused by Cystic Fibrosis on the White-men in Washington. At least 97% of the cystic fibrosis cases on men have the infertile condition but not sterile, because an obstruction occurs on ductus afferent and there is no development of *ductus different*, and as its effect the azoospermia will potentially occur and further will cause the infertility, so that it can reduce the rate of pregnancy.

The determination of optimal output from PCR optimization to obtain the location of ΔF 508-T mutant on CBAVD patients in Indonesia is conducted pursuant to the gene target. The Influence of various factors as the indicator specifying the mutation of ΔF 508-T mutant needs to be considered in making a decision for the preliminary research on CBAVD in Indonesia. Output of this research proves the 3 different primaries, starting from the holding on the fourth cycle and an increase continuously occurs till the 40^{th} cycle as an illustration of cDNA profile of the CBAVD patients. This research also proves that the CBAVD congenital defect on Indonesian people have the chain of DNA gene CFTR length at about 400 base pair (400bp). Output of this study proves that the abnormal congenital defect of the CBAVD on the Indonesian people has the chain of DNA gene CFTR at the range of 400 base pair (400bp), whereas the European people have 600 base pair (600bp). The difference in the output of this PCR is possibly influenced by various factors, namely : total amount of samples being researched, research implementation technique covering the duration and temperature during annealing, cycling and replication. Output of the SDS-PAGE analysis to determine the weight of CFTR protein molecule is more or less 190-250 kDa, 170-180 kDa, 140-160 kDa and 120 kDa. The long term objective of this research is to know how much is the base pair of CBAVD case in Indonesia expected to become the prototype to repair the gene undergoing the mutation as the result of congenital defect. The success of this study can give solution to the problem of CBAVD disease non the congenital defect due to the mutation of ΔF 508-T gene coding the CFTR.