mutations to be in between (9-21%) in patients with AML [2,5,11-13]. Discrepancy in RAS mutation frequency among various reports result from fact that criteria for selection of AML patients differ between various studies, N-RAS frequency in studies analyzed only denovo AML was lower than studies select AML that arose from proven MDS which is more frequently associated with N-RAS mutations [11]. Also the difference in RAS mutation frequency may explained by number of cases involved, method of screening, number of exon examined (codons 12, 13 in exon 1, codon 61 in exon 2) and type of RAS mutation (N, K and H-RAS) analyzed [13]. All N-RAS mutation detected in codon 12 (100%) and no mutation detected in codon 13, these finding were in agreement with previous studies [5,11-14].

Although that HphI enzyme digested the unamplified DNA, it failed to digest a 3' end of the amplified DNA (that served as a control for enzyme function). Current study suggested that this negative result is not due to failure of the primer system to detect mutations in the digested PCR product but the predominance of digestion resistant band as mentioned in previous report. Bashey and Todd studies describe an overrepresentation of the singly digested band, which is caused by the formation of restriction enzyme resistant hetero-duplexes between mutant and normal strands which are mismatched at a single base only [6,15]. In addition to that, the reverse Allele specific restriction analysis (ASRA) method described by Todd and Iland fails to demonstrate the presence or absence of wild type alleles, since a digestion resistant band merely indicates the lack of a specific mutation rather than the presence of wild type sequences [16].

Analyses revealed a statistically significant association between bone marrow blast percentage, WBC count and N-RAS mutation (P = 0.025, P = 0.033 respectively), however no significant differences had been found between the two groups with respect to age, gender, platelet count, hematocrit percentage and clinical outcomes. These findings were in agreement with those reported in previous literatures [2,5,11,14,17,18].

Mutation of the N-RAS gene affects the biology of AML. Transfection of various cell types with mutant RAS genes has been shown to stimulate secretion of interleukin-3, granulocyte, and granulocytemacrophage colony stimulating factors leading to autonomous growth through an autocrine mechanism, increasing peripheral WBC count [19].

The highest frequency of N-RAS mutation in M4 in current study corresponded with most of the previously published studiesm [5,11,13]. N-RAS mutation is most likely a postinitiation event contributing to the progression/proliferation of sub-clones in AML, selection and expansion of RAS mutant clones may provide a differentiative stimulus toward the monocytic lineage [2], Van Kamp study also suggested that N-RAS mutation preferentially influences hematopoiesis to myelomonocytic differentiation or myelo-monocytic cells are more susceptible for acquiring an N-RAS mutation since N-RAS mutations are more likely to develop in cells of myelomonocytic differentiation [20]. This may be consistent with the overrepresentation of RAS mutation in M4/M5 FAB types.

The low frequency of N-RAS mutation in M3 (10%) in current study corresponded with Bowen study, N-RAS mutation is relatively underrepresented in M3 where FLT3 ITD is overrepresented, both RAS mutation and FLT3 ITD are rarely present in the same tumor [2].

Current study showed that response to induction therapy was comparable to Alwan study and Lowenberg study were reported CR rate to be (70 - 80%) [8,9].

CR rate in mutant N-RAS patients was lower than wild type N-RAS patients, but the difference was not significant (P = 0.414). Published reports addressing the clinical significance of RAS mutations in patients with AML are inconclusive. Whereas some studies observed that the presence of N-RAS mutation did not significantly influence CR rate [2,15]. Others observed a significantly lower CR rate compared with patients without N-RAS mutation [12,21]. Third